Indian J Anim Health (2025), 64(1) - Special Issue: 55-65
DOI: https://doi.org/10.36062/ijah.2025.01925

Review Article

Phytotherapy as a natural alternative to antibiotics in aquaculture

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Abstract

The aquaculture industry, despite its significant economic contributions, faces considerable challenges from infectious diseases and the growing threat of antimicrobial resistance (AMR). Phytotherapy, the use of plant-derived bioactive compounds, presents a promising alternative to conventional pharmaceuticals for disease management. Medicinal plants have demonstrated antiparasitic, antibacterial, and antifungal properties, enhancing fish immunity and overall health. Incorporating herbal supplements into aqua feeds can reduce dependence on synthetic chemotherapeutics, mitigating environmental risks and supporting sustainable aquaculture practices. Additionally, phytotherapy has been shown to improve growth performance, bolster disease resistance, and enhance fish welfare, ultimately leading to increased production efficiency. With rising consumer demand for sustainably farmed seafood, integrating phytotherapy into aquaculture can enhance the industry's sustainability and market competitiveness. This review explores the potential of phytotherapy in revolutionizing disease management strategies and promoting environmentally responsible aquaculture.

Keywords: Antimicrobial Resistance, Aquaculture, Fish Immunity, Phytotherapy

Highlights

- Phytotherapy has antiparasitic, antibacterial, and antifungal effects in humans and animals
- Plant-derived compounds can enhance fish health and immune responses
- Phytotherapy can reduce reliance on chemotherapeutic parasiticides, minimizing environmental risks
- Herbal supplements can improve growth performance, immune response, and disease resistance in fish

INTRODUCTION

Global aquaculture production reached a record 130.9 million tonnes in 2022, valued at USD 313 billion. This comprised 94.4 million tonnes of aquatic animals and 36.5 million tonnes of algae. Asia dominated the sector, contributing 91.4% of the global output, followed by Latin America and the Caribbean (3.3%), Europe (2.7%), Africa (1.9%), North America (0.5%), and Oceania (0.2%). The top ten producing countries - China, Indonesia, India, Vietnam, Bangladesh, the Philippines, South Korea, Norway, Egypt, and Chile - collectively accounted for 89.8% of the total production (Dongyu, 2024). The growth of the aquaculture industry is hindered by various challenges, with infectious diseases being a significant factor. Disease outbreaks often stem from poor fish health management, including inadequate water quality, insufficient nutrition, improper sanitation, and high stocking densities (Chong *et al*., 2020).

The use of pharmaceuticals in aquaculture, including antimicrobials, disinfectants, pesticides, and other chemicals, faces an uncertain future due to their potential adverse impacts on the aquatic environment, as well as on animals and humans (Rico and Van den Brink, 2014). Currently, approved antibiotics for use in aquaculture include tetracycline, penicillin, quinolones, sulphonamides, and trimethoprim (Conti *et al*., 2015). In contrast, the use of chloramphenicol, nitrofurans, vancomycin, dimetridazole, and cimaterol is banned due to their harmful effects, such as carcinogenicity, bone marrow suppression, aplastic anemia, and acute nephrotoxicity (Bondad-Reantaso *et al*., 2012; Conti *et al*., 2015).

Herbal medicine has garnered significant interest in aquaculture since the 1990s, primarily due to the bioactive compounds they contain, such as flavonoids, alkaloids, terpenoids, tannins, polysaccharides, and essential oils. These compounds serve not only as

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chemotherapeutics but also as feed additives to boost the immune response of aquatic species (Tadese *et al*., 2020; Zhu, 2020; Amiruddin *et al*., 2021). Research has demonstrated that medicinal plants possess a variety of biological properties, including stress-relieving, antimicrobial, antiviral, and antiparasitic effects. Additionally, they are characterized by low toxicity (Stratev *et al*., 2017; Zhu, 2020) and offer environmental and economic benefits (Cawthorn and Hoffman, 2015).

Many plant species have been used as medicinal plants for humans since ancient times. Plants synthesize diverse chemical compounds to defend against insects, fungi, pathogens, and herbivores. Numerous bioactive substances have been identified for their therapeutic potential. In developing countries, herbal medicines derived from plants are commonly used for treatment. For instance, in Indonesia, herbal medicine is a well-known approach for healing. However, the bioactive substances or secondary metabolites found in a given plant species can vary significantly in both type and concentration, depending on factors such as soil composition, climate, plant age, and other ecological conditions (Effendi *et al*., 2022).

Immunomodulatory effects of phytogenic compounds in aquacultured fish

The immune system comprisesinnate (non-specific or natural) immunity and adaptive (specific or acquired) immunity, with the innate immune system serving as the first line of defense against pathogens (Carbone and Faggio, 2016; Ahmadifar *et al*., 2019). The innate immune system can be further divided into epithelial barriers, humoral factors, and cellular components (Magnadottir, 2010; Bruce and Brown, 2017). In fish, mucus, gills, and scales constitute the primary physical barriers. Fish mucus containslectins, immunoglobulins, lysozymes (LYZ), and complement proteins (Uribe *et al*., 2011; Elumalai *et al*., 2019). Integumentary secretions also harbor antimicrobial peptides that lyse bacterial cell walls (Uribe *et al*., 2011; Vallejos-Vidal *et al*., 2016).

The humoral components of fish innate immunity include lysozymes (LYZ) and the complement system, while the primary cellular components consist of monocytes, macrophages, and granulocytes (Magnadottir, 2006, 2010; Van Hai, 2015; Burgos-Aceves *et al*., 2019). Other key players include transferrin, antimicrobial peptides, and antiproteases. Physical barriers such as the epidermis, mucosal surfaces, and scales act as the first line of defense, preventing the intrusion of foreign agents (Esteban, 2012). The fish gut has gained considerable focus in immunity studies (Caipang and Lazado, 2015) due to its role as a primary pathway for pathogen entry (Birkbeck and Ringø, 2005).

The mucosal immune system in fish relies heavily on gut-associated lymphoid tissue (GALT), which serves as a critical defense mechanism (Reverter *et al*., 2014; Lauriano *et al*., 2023). The posterior intestine is immunologically active, containing B cells, T cells, macrophages, and granulocytes (Magnadottir, 2010). Innate immune responses in fish include the generation of reactive oxygen and nitrogen species, as well as the activity of various enzymes, notably the extensively studied peroxidase. Activation is essential for immune cells to perform their functions. In adaptive immunity, B-cell receptors recognize antigens, triggering memory B-cell proliferation. This, in turn, activates T lymphocytes and triggers the release of cytokines (Reverter *et al*., 2014).

To defend against pathogens such as bacteria, parasites, and viruses, fish utilize phagocytosis as a cornerstone of their innate immunity. The lectin, classical, and alternative pathways further enhance phagocytosis via pathogen opsonization (Boshra *et al*., 2006; Elumalai *et al*., 2019). Non-specific cytotoxic cells, functionally similar to mammalian natural killer cells, have been identified in fish species such as catfish (*Clarias gariepinus*), rainbow trout (*Oncorhynchus mykiss*), common carp (*Cyprinus carpio*), Nile tilapia (*Oreochromis niloticus*), gilthead seabream (*Sparus aurata*), and European sea bass (*Dicentrarchus labrax*) (Ortuño *et al*., 2002).

Macrophages and neutrophils, key phagocytic cells in fish, eliminate bacteria through mechanisms like respiratory bursts. They also harborhydrolytic enzymes and lysozymes (LYZ). Tumor necrosis factor activates macrophages in species like sea bream, goldfish (*Carassius auratus*), and catfish, boosting bacterial phagocytosis (Uribe *et al*., 2011). Additionally, cytokines such as interferons α and β play a vital role in defending against viral infections. For instance, interferons in Atlantic salmon (*Salmo salar*) have been found to induce antiviral activity against infectious pancreatic necrosis virus (Jensen and Robertsen, 2002).

Fish adaptive immunity effectively recognizes pathogens and establishes immunological memory (Secombes *et al*., 2005; Randelli *et al*., 2008). Immunostimulants enhance both innate and adaptive immunity, boosting disease resistance in fish and shellfish (Deivasigamani and Subramanian *et al*., 2016; Ringø *et al*., 2012). While these substances can be administered via injection or as dietary supplements, the latter is generally preferred for its practicality and reduced stress on. Although injection allows for precise dosing, it is labor-intensive and stressful due to the required handling and manipulation (Selvaraj *et al.*, 2005).

Antimicrobial resistance in aquaculture

Antimicrobial resistance (AMR) is a global concern, causing an estimated 1.27 million deaths in 2019, with disproportionate impacts on low- and middle-income countries. Aquatic ecosystems act as major reservoirs and transmission pathways for AMR (Murray *et al.*, 2022). The use of antibiotics directly in aquaculture systems is not the only factor contributing to the global spread of AMR; integrated fish farming systems also play a significant role. These systems - especially prevalent in Asia and Africa - are key AMR transmission pathways (Watts *et al.*, 2017). Depending on the biodegradability, initial concentration, and physical and chemical properties, fish feces and uningested food may maintain the antimicrobial residues (Burridge *et al.*, 2010). This prolonged selective pressure promotes the emergence of antimicrobial resistance determinants. The antibiotic environment's fluctuation compels the bacteria to adapt, which in turn leads to their selection for survival through a variety of mechanisms (Baquero *et al.*, 1998). Selection pressure alters aquatic biodiversity through genetic shifts that either generate new AMR variants or replace susceptible populations with resistant ones (Cabello *et al.*, 2013). According to Chiew *et al.* (1998), the main drawback of selection pressure is that, if resistance is developed, the determinants may persist in the community even in the absence of effective antibiotics. The use of antibiotics in cultivated open systems, like ponds, raises the possibility that AMR genes may persist and spread throughout the system because there is less frequent water exchange and more time for bacterial adaptation (Neela *et al.*, 2015). Aeromonad pathogens on the gut and skin of treated fishes and biofilms developed multidrug resistance against streptomycin, sulfamethoxazole, quinolones and fluoroquinolones, oxytetracycline, florfenicol, chloramphenicol, and trimethoprim after receiving flumequine treatment in pond water and rainbow trout farms. This facilitated the transfer of pertinent genes to broader aquatic environments during harvest (Naviner *et al.*, 2011).

Different types of herbs are used in aquaculture and their properties

The efficacy of medicinal plants is closely linked to the abundance of bioactive compounds, which are influenced by various factors such as geographical location, the specific plant part utilized, and the age of the harvested plant. Additionally, the type of plant material used (e.g., dried powdered plant or extract) plays a significant role in determining the metabolite profile and biological potential. Reverter *et al.* (2021) noted that powdered plants were the most commonly employed material, followed by ethanolic extracts, essential oils (EO), and aqueous extracts. This preference reflects production cost-effectiveness and safety considerations. Alcoholic solvents are preferred over aqueous due to their intermediate polarity, facilitating broader-spectrum phytochemical extraction and greater bioactivity. However, solutions rich in bioactive molecules may sometimes exhibit toxic effects on treated fish and crustaceans. The biological activity of plant extracts largely depends on the extraction methods employed, including factors such as solvent polarity, equipment, and temperature, which influence the composition and abundance of bioactive compounds in the extract. Variations in the availability of phytochemicals can significantly affect therapeutic outcomes. Beyond plant extracts and powdered forms, essential oils (EO) are also widely utilized as feed supplements in aquaculture due to their low toxicity. Moreover, EO has been recognized as safe (GRAS) by the US Food and Drug Administration (FDA, 2016) (Table 1).

Phytotherapy as an alternative to antibiotics in aquaculture

Phytotherapy involves treating diseases with medicinal plant-based products for prevention, cure, or relief (Reverter *et al.*, 2014). Their antiparasitic, antibacterial, and antifungal efficacy has been demonstrated in both human and veterinary medicine (Silva and Fernandes-Júnior, 2010). While herbal medicines have long been used in human health, their application in aquaculture is gaining attention as safer alternatives to conventional drugs, which threaten aquatic ecosystems. Research on plant-derived antimicrobials has driven studies on controlling parasitic infections in humans, animals, and fish (Abd El-Galil and Aboelhadid, 2012). In aquaculture, their use can reduce reliance on chemical parasiticides, promoting more sustainable fish farming with lower environmental impact. These natural treatments help manage fish diseases, preventing mortality and

Table 1. Different types of herbs are used in aquaculture and their properties

Scientific Name	Common Name	Part Used	Bioactive Compounds	Properties	References
Azadirachta indica	Neem	Leaf extract	Azadirachtin, nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, gedunin, salannin, and quercetin	Antibacterial, antifungal, antimicrobial, antioxidant, anti-inflammatory	Islamy *et al.*, 2024
Scutellaria baicalensis	Chinese skullcap	Aerial part	Baicalin, baicalein, 7-O-glucuronide, oroxylin A	Antimicrobial, antioxidant, anticancer, anti-inflammatory	Xia *et al.*, 2023
Castanea sativa	Sweet chestnut	Shell (phenolic extract)	Trigalloyl-HHDP-glucose, gallic acid, quercetin	Antibacterial, antioxidant	Imperatore *et al.*, 2023
Pandanus tectorius	Screw pine	Leaf powder extract	p-Hydroxybenzaldehyde, syringaldehyde, E-ferulaldehyde, E-sinapinaldehyde, vanillin, 5-hydroxymethylfurfural	Antibacterial, antioxidant	Cheng *et al.*, 2022
Aloe vera	Aloe vera	Leaves	7-Hydroxyaloin A, 7-hydroxyaloin B, 8-O-methyl-7-hydroxyaloin A, S-O-methyl-7-hydroxyaloin B	Antibacterial, antifungal, antiviral	Amri *et al.*, 2022
Elaeagnus angustifolia	Russian olive	Leaf extract	Cyanidin-3-O-glucoside, gallic acid, anthocyanin	Antimicrobial, antioxidant, antimutagenic	Hoseini *et al.*, 2021
Coffea arabica	Arabian coffee	Coffee silver skin	Chlorogenic acids, caffeine, trigonelline, melanoidins, diterpenes	Antibacterial	Van Doan *et al.*, 2021
Citrus limon	Lemon	Lemon peels	Caffeoyl N-tryptophan, hydroxycinnamoyl-O-glucoside acid, vicenin 2, eriocitrin, kaempferol-3-O-rutinoside, quercetin-3-rutinoside	Antibacterial, antifungal	Harikrishnan *et al.*, 2020
Nigella sativa	Black cumin	Seeds	Thymoquinone, thymohydroquinone, dithymoquinone, p-cymene, carvacrol, 4-terpineol, t-anethole, sesquiterpene, a-pinene, thymol	Antibacterial	Latif *et al.*, 2020
Arum maculatum	Cuckoo pint	Leaves	1,1-Diphenyl-2-picrylhydrazyl (DPPH),	Antimicrobial, antioxidant,	Farahmandfar *et al.*, 2019

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Scientific Name	Common Name	Part Used	Bioactive Compounds	Properties	References
			β-Carotene, tocopherols	antibacterial, antimutagenic, anticarcinogenic, cardioprotective	
Thymus vulgaris	Common thyme	Oil	Borneol, carvacrol, cymol, linalool, thymol, tannin, apigenin, luteolin, saponins, triterpenic acid	Antibacterial, antifungal, antioxidant	Gedikoðlu *et al.*, 2019
Achillea cucullata	Gandrain	Oil	Camphor, 1,8-cineole, isoborneol	Antioxidant, antibacterial, antimicrobial, enzyme-inhibition	Eruygur *et al.*, 2019
Anisomeles malabarica	Malabar catmint	Leaves	β-Sitosterol, ovatodiolide, anisomelic acid, malabarie acid, anisomelol, triterpene betulinic acid	Antioxidant, antibacterial	Krishna *et al.*, 2019
Cynara cardunculus	Cardoon	Oil	5-O-Caffeoylquinic acid, 3,5-O-dicaffeoylquinic acid, luteolin-7-O-glucoside, luteolin-7-O-malonylhexoside, fatty acids	Antioxidant, anti-inflammatory, antifungal, antibacterial	Scavo *et al.*, 2019
Melocanna baccifera	Muli bamboo	Leaf	β-Sitosterol, E-phytol, β-amyrin, syringic acid, blumenol B, tianshic acid	Antifungal, antibacterial, antiprotozoal, antitussive, immunomodulatory	Khan *et al.*, 2018
Thymus linearis	Himalayan thyme	Oil	Thymol, carvacrol, thymyl acetate, p-caryophyllene	Antimicrobial, antioxidant, antiseptic	Shirazi, 2018
Excoecaria agallocha	Mangrove	Leaf	Squalene, tocopherol, terpenoids	Antimicrobial, antibacterial, immunomodulatory	Laith *et al.*, 2017
Mentha piperita	Peppermint	Oil	Menthone, iso-menthone, menthol, germacrene D, α-pinene, limonene, 1, 8-cineole	Antimicrobial, antibacterial, immunostimulant	Adel *et al.*, 2015
Ocimum sanctum	Tulsi	Leaves	Ursolic acid, oleanolic acid, salrigenin	Antioxidant, antimicrobial, antibacterial, antidiabetic, antiviral	Das *et al.*, 2015
Citrus medica	Fingered citron	Fruit	Limonene, geranial, neral	Antifungal, antibacterial	Hu *et al.*, 2014

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Scientific Name	Common Name	Part Used	Bioactive Compounds	Properties	References
Zingiber officinale	Ginger	Root	Zingiberene, p-bisabolene, α-farnesene, p-sesquiphellandrene, α-curcumene, 6-gingerol, 6-shogaol	Antioxidant, antibacterial, anti-inflammatory	Hassanin *et al*., 2014
Cinnamomum cassia	Chinese cinnamon	Tree bark	Cinnamaldehyde, cinnamon oil, eugenol, salicylaldehyde, trans-cinnamic acid	Antioxidant, anti-inflammatory, antibacterial	Ji *et al*., 2012
Eriobotrya japonica	Japanese medlar	Leaves	Corosolic acid, 3-epicorosolic acid, euscaphic acid, oleanolic acid, maslinic acid, methyl arjunolate, betulinic acid	Antioxidant, anti-inflammatory, antibacterial	Kim *et al*., 2012
Tinospora cordifolia	Guduchi	Leaves	Berberine, choline, tinosporin, tinocordiside, furanolactone, â-sitosterol	Antibacterial	Alexander *et al*., 2010
Withania somnifera	Ashwagandha	Root	Withanolides, withasomnine, somnirol, somnitol, withanic acid, phytosterol, ipuranol	Antibacterial	Sharma *et al*., 2010
Toona sinensis	Chinese cedar	Leaves	Ursolic acid, betulinic acid, cedrellin, phytol, scopoletin	Antibacterial, antiviral, antioxidant, anticancer, anti-inflammatory	Wu *et al*., 2010
Punica granatum	Pomegranate	Leaves	Ellagic acid, gallic tannins	Antiviral, antibacterial	Harikrishnan *et al*., 2010
Thymus daenensis	Thyme	Oil	Thymol, p-cymene, 1,8-cineole, ã-terpinene, carvacrol	Antiseptic, antimicrobial, antispasmodic, antioxidant, antitussive	Pirbalouti *et al*., 2009
Indigofera suffruticosa	Indian indigo	Leaves	Syringic acid, p-coumaric acid, vanillin, syringaldehyde, salicylic acid, quercetin, isoliquiritigenin, formononetin	Antibacterial	Leite *et al*., 2006
Camellia sinensis	Tea plant	Leaves, buds	Catechins, epicatechins, theaflavins, flavonol glycosides, L-theanine, caffeine, theobromine	Antiparasitic, antibacterial	Suzuki *et al*., 2006
Allium sativum	Garlic	Tuber	Allicin, alliin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, ajoene, S-allyl-cysteine	Hypolipidemic, antibacterial, antihypertensiv, hepatoprotective	Sahu *et al*., 2007

(Source: Semwal *et al*., 2023)

economic losses. Interest in phytotherapeutics for treating fish parasites emerged several years ago (Ekanem *et al*., 2004a, b; Steverding *et al*., 2005). Aquaculture phytotherapy primarily reduces chemotherapeutic dependence, simultaneously mitigating environmental risks, controlling diseases, and preventing mortality-related economic losses (Harikrishnan, 2003). Herbal remedies in fish health management are administered as decoctions (individually), concoctions (combined), or in conjunction with other medications (Harikrishnan, 2003). The primary rationale behind incorporating phytotherapy in aquaculture is its potential to minimize reliance on chemotherapeutic parasiticides, thereby lowering environmental risks. Additionally, it aids in treating fish diseases, reducing mortality, and preventing economic losses. The use of phytotherapeutics also reduces the likelihood of fish developing disease resistance (Kulkarni *et al*., 2013) due to their multi-target mode of action (Bakkali *et al*., 2008). Plants biosynthesize diverse bioactive secondary metabolites (SMs) for environmental adaptation, stress tolerance, and pathogen defense. These metabolites include alkaloids, essential oils, phenolics, saponins, terpenes, and carbohydrates (Varijakzhan *et al*., 2020).The overuse of antibiotics in aquaculture has raised significant concerns regarding antimicrobial resistance, environmental contamination, and food safety. As a sustainable alternative, phytotherapy-the use of plant-derived compounds for disease prevention and treatment-has gained attention for its effectiveness in enhancing fish health while mitigating these concerns.

Conclusion

In conclusion, while the global aquaculture industry has made significant strides in production and economic contribution, it must navigate the challenges posed by infectious diseases and antimicrobial resistance. The exploration of herbal medicine as an alternative to traditional pharmaceuticals offers a promising pathway to enhance fish health and immune responses, potentially transforming the industry's approach to disease management and sustainability. By embracing innovative solutions rooted in natural remedies, the aquaculture sector can work towards a more resilient and responsible future. Additionally, the use of herbal supplements may promote overall health and growth in fish, leading to improved production outcomes. Furthermore, as consumers increasingly seek sustainably sourced and environmentally friendly seafood options, the adoption of herbal medicine could enhance the industry's reputation and marketability.

Conflict of interest: The authors declare that they have no conflicts of interest related to this work. No financial, personal, or professional affiliations have influenced the content, analysis, or conclusions presented in this review.

Author's contribution: SP: Conceptualization; SP, GS, SV, AS: Writing - original draft; SP, SS, SV, PKT, TD: Writing - review & amp, editing SV: Visualization. All authors have read and approved the final version of the manuscript.

Data availability statement: This review paper is based on previously published literature and does not include any new data generated or analyzed by the authors. All data supporting the findings of this study are available in the referenced publications. Further inquiries can be directed to the corresponding author.

REFERENCES

Abd El-Galil MA and Aboelhadid SM, 2012. Trials for the control of trichodinosis and gyrodactylosis in hatchery reared *Oreochromis niloticus* fries by using garlic. Vet Parasitol, 185(2-4): 57-63, doi: 10.1016/j.vetpar.2011.10.035

Adel M, Amiri AA, Zorriehzahra J, Nematolahi A and Esteban MÁ, 2015. Effects of dietary peppermint (*Mentha piperita*) on growth performance, chemical body composition and hematological and immune parameters of fry Caspian white fish (*Rutilus frisiikutum*). Fish Shellfish Immunol, 45(2): 841-847, doi: 10.1016/j.fsi.2015.06.010

Ahmadifar E, Sheikhzadeh N, Roshanaei K, Dargahi N and Faggio C, 2019. Can dietary ginger (*Zingiber officinale*) alter biochemical and immunological parameters and gene expression related to growth, immunity and antioxidant system in zebrafish (*Danio rerio*)? Aquaculture, 507: 341-348, doi: 10.1016/j.aquaculture.2019.04.049

Alexander CP, Kirubakaran CJW and Michael RD, 2010. Water soluble fraction of *Tinospora cordifolia* leaves enhanced the non-specific immune mechanisms and disease resistance in *Oreochromis mossambicus*. Fish Shellfish Immunol, 29(5): 765-772, doi: 10.1016/j.fsi.2010.07.003

Amiruddin WM, Sukri SAM, Al-Amsyar SM, Rusli ND, Mat KB *et al*., 2021. Application of herbal plants in giant freshwater prawn: A review on its opportunities and limitation. In: IOP Conference Series: Earth and Environmental Science, 756: No.1, p. 012022. IOP Publishing, doi: 10.1088/1755-1315/756/1/012022

Amri A, Bouraoui Z, Balbuena-Pecino S, Capilla E, Gharred T *et al*., 2022. Dietary supplementation with Aloe vera induces hepatic steatosis and oxidative stress together with a disruption of cellular signaling pathways and lipid metabolism related genes' expression in gilthead sea bream (*Sparus aurata*). Aquaculture, 559, 738433, doi: 10.1016/j.aquaculture.2022.738433

Bakkali F, Averbeck S, Averbeck D and Idaomar M, 2008. Biological effects of essential oils-A review. Food Chem Toxicol, 46(2): 446-475, doi: 10.1016/j.fct.2007.09.106

Baquero F, Negri MC, Morosini MI and Blázquez J, 1998. Antibiotic-selective environments. Clin Infect Dis, 27(Supplement_1): S5-S11, doi: 10.1086/514916

Birkbeck TH and Ringø E, 2005. Pathogenesis and the gastrointestinal tract of growing fish. Biol Grow Anim, 2: 208-234, doi: 10.1016/S1877-1823(09)70043-8

Bondad-Reantaso MG, Arthur JR and Subasinghe RP, 2012. Improving biosecurity through prudent and responsible use of veterinary medicines in aquatic food production. FAO Fish Aquac Technical Paper, No 547, Rome, FAO. pp207

Boshra H, Li J and Sunyer JO, 2006. Recent advances on the complement system of teleost fish. Fish Shellfish immunol, 20(2): 239-262, doi: 10.1016/j.fsi.2005.04.004

Bruce TJ and Brown ML, 2017. A review of immune system components, cytokines, and immunostimulants in cultured Finfish species. Open J Anim Sci, 7(03): 267, doi: 10.4236/ojas.2017.73021

Burgos-Aceves MA, Lionetti L and Faggio C, 2019. Multidisciplinary haematology as prognostic device in environmental and xenobiotic stress-induced response in fish. Sci Total Environ, 670: 1170-1183, doi: 10.1016/j.scitotenv.2019.03.275

Burridge L, Weis JS, Cabello F, Pizarro J and Bostick K, 2010. Chemical use in salmon aquaculture: a review of current practices and possible environmental effects. Aquaculture, 306(1-4): 7-23, doi: 10.1016/j.aquaculture.2010.05.020

Cabello FC, Godfrey HP, Tomova A, Ivanova L, Dölz H *et al*., 2013. Antimicrobial use in aquaculture re examined: its relevance to antimicrobial resistance and to animal and human health. Environ Microbiol, 15(7): 1917-1942, doi: 10.1111/1462-2920.12134

Caipang CMA and Lazado CC, 2015. Nutritional impacts on fish mucosa: immunostimulants, pre-and probiotics. In: Mucosal Health in Aquaculture, by B. H. Beck and E. Peatman. Academic Press,London, pp 211-272. doi: 10.1016/B978-0-12-417186-2.00009-1

Carbone D and Faggio C, 2016. Importance of prebiotics in aquaculture as immunostimulants. Effects on immune system of *Sparus aurata* and *Dicentrarchus labrax*. Fish Shellfish Immunol, 54: 172-178, doi: 10.1016/j.fsi.2016.04.011

Cawthorn DM and Hoffman LC, 2015. The bushmeat and food security nexus: A global account of the contributions, conundrums and ethical collisions. Food Res Int, 76: 906-925, doi: 10.1016/j.foodres.2015.03.025

Cheng C, Park SC and Giri SS, 2022. Effect of *Pandanus tectorius* extract as food additive on oxidative stress, immune status, and disease resistance in *Cyprinus carpio*. Fish Shellfish Immunol, 120: 287-294, doi: 10.1016/j.fsi.2021.12.004

Chiew YF, Yeo SF, Hall LM and Livermore DM, 1998. Can susceptibility to an antimicrobial be restored by halting its use? The case of streptomycin versus Enterobacteriaceae. J Antimicrob Chemother, 41(2): 247-251, doi: 10.1093/jac/41.2.247

Chong CM, Murthy AG, Choy CY and Lai KS, 2020. Phytotherapy in aquaculture: Integration of endogenous application with science. J Environ Biol, 41: 1204-1214, doi: 10.22438/jeb/41/5(SI)/MS_12

Conti GO, Copat C, Wang Z, D'Agati P, Cristaldi A *et al*., 2015. Determination of illegal antimicrobials in aquaculture feed and fish: an ELISA study. Food Control, 50: 937-941, doi: 10.1016/j.foodcont.2014.10.050

Das R, Raman RP, Saha H and Singh R, 2015. Effect of *Ocimum sanctum* Linn. (Tulsi) extract on the immunity and survival of *Labeorohita* (Hamilton) infected with *Aeromonas hydrophila*. Aquac Res, 46(5): 1111-1121, doi: 10.1111/are.12264

Deivasigamani B and Subramanian V, 2016. Applications of immunostimulants in aquaculture: A review. Int J Curr Microbiol Appl Sci 5(9): 447-453, doi: 10.20546/ijcmas.2016.509.048

Dongyu Q, 2024. The State of World Fisheries and Aquaculture-blue Transformation in Action. State World Fish Aquac, Blue Transformation in action, Rome. R1-232, doi: 10.4060/cd0683en

Effendi I, Yoswaty D, Syawal H, Austin B, Lyndon AR *et al*., 2022. The use of medicinal herbs in aquaculture industry: A review. Curr Aspects Pharma Res Dev, 7: 7-20, doi: 10.9734/bpi/caprd/v7/2190C

Ekanem AP, Obiekezie A, Kloas W and Knopf K, 2004a. Effects of crude extracts of *Mucuna pruriens* (Fabaceae) and *Carica papaya* (Caricaceae) against the protozoan fish parasite *Ichthyophthirius multifiliis*. Parasitol Res, 92: 361-366, doi: 10.1007/s00436-003-1038-8

Ekanem AP, Wang M, Simon JE, Obiekezie AI and Morah F, 2004b. In vivo and in vitro activities of the seed extract of *Piper guineense* Schum. and Thonn. against skin and gill monogenean parasites of goldûsh (*Carassius auratus*). Phytotherapy Research,18(10): 793-797, doi: 10.1002/ptr.1550

Elumalai P, Rubeena AS, Arockiaraj J, Wongpanya R, Cammarata M *et al*., 2019. The role of lectins in finfish: a review. Rev Fish Sci Aquac, 27(2): 152-169, doi: 10.1080/23308249.2018.1520191

Eruygur N, Koçyiðit UM, Taslimi P, Ataþ MEHMET, Tekin M *et al*., 2019. Screening the in vitro antioxidant, antimicrobial, anticholinesterase, antidiabetic activities of endemic *Achillea cucullata* (Asteraceae) ethanol extract. S Afr J Bot, 120: 141-145, doi: 10.1016/j.sajb.2018.04.001

Esteban MA, 2012. An overview of the immunological defenses in fish skin. Int Sch Res Notice, 2012(1): 853470, doi: 10.5402/2012/853470

Farahmandfar R, Esmaeilzadeh Kenari R, Asnaashari M, Shahrampour D and Bakhshandeh T, 2019. Bioactive compounds, antioxidant and antimicrobial activities of *Arum maculatum* leaves extracts as affected by various solvents and extraction methods. Food Sci Nutr, 7(2): 465-475, doi: 10.1002/fsn3.815

FDA (Food and Drug Administration of the United Nations), 2016. Electronic code of federal regulations (e-CFR). Part 182-substances generally recognized as safe, Section 182.20-essential oils, oleoresins (solvent-free), and natural extractives (including distillates). Title 21, Volume 3. Revised as of September 1, 2016. https:// www. accessdata. fda. gov/ scrip ts/ cdrh/ cfdocs/ cfcfr/ CFRSe arch. cfm? fr= 182. 20

Gedikoðlu A, Sökmen M, and Çivit A, 2019. Evaluation of *Thymus vulgaris* and *Thymbra spicata* essential oils and plant extracts for chemical composition, antioxidant, and antimicrobial properties. Food Sci Nutr, 7(5): 1704-1714, doi: 10.1002/fsn3.1007

Harikrishnan R, Heo J, Balasundaram C, Kim MC, Kim JS *et al*., 2010. Effect of *Punica granatum* solvent extracts on immune system and disease resistance in *Paralichthys olivaceus* against lymphocystis disease virus (LDV). Fish Shellfish Immunol, 29(4): 668-673, doi: 10.1016/ j.fsi.2010.07.006

Harikrishnan R, Rani MN, and Balasundaram C, 2003. Hematological and biochemical parameters in common carp, *Cyprinus carpio*, following herbal treatment for *Aeromonas hydrophila* infection. Aquaculture, 221(1-4): 41-50, doi: 10.1016/S0044-8486(03)00023-1

Harikrishnan R, Thamizharasan S, Devi G, Van Doan H, Kumar TTA *et al*., 2020. Dried lemon peel enriched diet improves antioxidant activity, immune response and modulates immuno-antioxidant genes in *Labeo rohita* against *Aeromonas sorbia*. Fish Shellfish Immunol, 106: 675-684, doi: 10.1016/j.fsi.2020.07.040

Hassanin ME, Hakim Y and Badawi M, 2014. Dietary effect of ginger (*Zingiber officinale* Roscoe) on growth performance, immune response of Nile tilapia (*Oreochromis niloticus*) and disease resistance against *Aeromonas hydrophila*. Abbassa Int J Aquac, 7: 35-52

Hoseini SM, Mirghaed AT, Iri Y, Hoseinifar SH, Van Doan H *et al*., 2021. Effects of dietary Russian olive, Elaeagnus angustifolia, leaf extract on growth, hematological, immunological, and antioxidant parameters in common carp, *Cyprinus carpio*. Aquaculture, 536, 736461, doi: 10.1016/j.aquaculture.2021.736461

Hu Y, Ji J, Ling F, Chen Y, Lu L *et al*., 2014. Screening medicinal plants for use against *Dactylogyrus intermedius* (Monogenea) infection in goldfish. J Aquatic Anim Health, 26(3): 127-136, doi: 10.1080/08997659. 2014.902872

Imperatore R, Orso G, Facchiano S, Scarano P, Hoseinifar SH *et al*., 2023. Anti-inflammatory and immunostimulant effect of different timing-related administration of dietary polyphenols on intestinal inflammation in zebrafish, *Danio rerio*. Aquaculture, 563, 738878, doi: 10.1016/ j.aquaculture.2022.738878

Islamy RA, Hasan V, Mamat NB, Kilawati Y and Maimunah Y, 2024. Immunostimulant evaluation of neem leaves againts non-specific immune of tilapia infected by *A. hydrophila*. Iraqi J Agric Sci, 55(3): 1194-1208, doi: 10.36103/dywdqs57

Jensen I, and Robertsen B, 2002. Effect of double-stranded RNA and interferon on the antiviral activity of Atlantic salmon cells against infectious salmon anemia virus and infectious pancreatic necrosis virus. Fish Shellfish Immunol, 13(3): 221-241, doi: 10.1016/S0165-2427(01)00406-8

Ji J, Lu C, Kang Y, Wang GX and Chen P, 2012. Screening of 42 medicinal plants for in vivo anthelmintic activity against *Dactylogyrus intermedius* (Monogenea) in goldfish (*Carassius auratus*). Parasitol Res, 111: 97-104, doi: 10.1007/s00436-011-2805-6

Khan MIR, Saha RK and Saha H, 2018. Muli bamboo (*Melocanna baccifera*) leaves ethanolic extract a non-toxic phyto-prophylactic against low pH stress and saprolegniasis in *Labeo rohita* fingerlings. Fish Shellfish Immunol, 74: 609-619, doi: 10.1016/ j.fsi.2017.11.047

Kim YK, Yeo J, Kim B, Ha M and Kim VN, 2012. Short structured RNAs with low GC content are selectively lost during extraction from a small number of cells. Molecular cell, 46(6): 893-895, doi: 10.1016/ j.molcel.2012.05.036

Krishna S, Chandrasekaran S, Dhanasekar D and Perumal A, 2019. GCMS analysis, antioxidant and antibacterial activities of ethanol extract of *Anisomeles malabarica* (L.) R. Br. ex. Sims leaves. Asian J Pharm Pharmacol, 5(1): 180-187, doi: 10.31024/ ajpp.2019.5.1.26

Kulkarni RR, Pawar PV, Joseph MP, Akulwad AK, Sen A *et al*., 2013. *Lavandula gibsoni* and *Plectranthus mollis* essential oils: chemical analysis and insect control activities against *Aedes aegypti*, *Anopheles sfttephensi* and *Culex quinquefasciatus*. J Pest Sci, 86: 713-718, doi: 10.1007/ s10340-013-0502-1

Laith AA, Mazlan AG, Effendy AW, Ambak MA, Nurhafizah WWI *et al*., 2017. Effect of *Excoecaria agallocha* on non-specific immune responses and disease resistance of *Oreochromis niloticus* against *Streptococcus agalactiae*. Res Vet Sci, 112: 192-200, doi: 10.1016/ j.rvsc.2017.04.020

Latif M, Faheem M, Asmatullah Hoseinifar SH, and Van Doan H, 2020. Dietary black seed effects on growth performance, proximate composition, antioxidant and histo-biochemical parameters of a culturable fish, rohu (*Labeo rohita*). Animals, 11(1): 48, doi: 10.3390/ani11010048

Lauriano ER, Alesci A, Aragona M, Pergolizzi S, Miller A *et al*., 2023. Immunohistochemistry of the gut-associated lymphoid tissue (GALT) in African Bonytongue (*Heterotis niloticus*, Cuvier 1829). Int J Mol Sci, 24(3): 2316, doi: 10.3390/ijms24032316

Leite SP, Vieira JR C, de Medeiros PL, Leite RMP, de Menezes Lima VL *et al.*, 2006. Antimicrobial activity of *Indigofera suffruticosa*. Evid Based Complement Altern Med, 3(2): 261-265, doi: 10.1093/ecam/nel010

Magnadottir B, 2006. Innate immunity of fish (overview). Fish Shellfish Immunol, 20(2): 137-151, doi: 10.1016/j.fsi.2004.09.006

Magnadottir B, 2010. Immunological control of fish diseases. Mar Biotechnol, 12: 361-379, doi: 10.1007/s10126-010-9279-x

Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR *et al.*, 2022. Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. Lancet, 399(10325): 629-655, doi: 10.1016/S0140-6736(21)02724-0

Naviner M, Gordon L, Giraud E, Denis M, Mangion C *et al.*, 2011. Antimicrobial resistance of *Aeromonas* spp. isolated from the growth pond to the commercial product in a rainbow trout farm following a flumequine treatment. Aquaculture, 315(3-4): 236-241, doi: 10.1016/j.aquaculture.2011.03.006

Neela FA, Banu MNA, Rahman MA, Rahman MA and Alam MF, 2015. Occurrence of antibiotic resistant bacteria in pond water associated with integrated poultry-fish farming in Bangladesh. Sains Malays, 44(3): 371-377, doi: 10.17576/jsm-2015-4403-08

Ortuño J, Cuesta A, Rodrŷìguez A, Esteban MA and Meseguer J, 2002. Oral administration of yeast, *Saccharomyces cerevisiae*, enhances the cellular innate immune response of gilthead seabream (*Sparus aurata* L.). Vet Immunol Immunopathol, 85(1-2): 41-50, doi: 10.1016/S0165-2427(01)00406-8

Pirbalouti AG, Taheri M, Raisee M, Bahrami HR and Abdizadeh R, 2009. In vitro antifungal activity of plant extracts on *Saprolegnia parasitica* from cutaneous lesions of rainbow trout (*Oncorhynchus mykiss*) eggs. J Food Agric Environ, 7, 94-6, doi: 10.1234/4.2009.1546

Randelli E, Buonocore F and Scapigliati G, 2008. Cell markers and determinants in fish immunology. Fish Shellfish Immunol, 25(4): 326-340, doi: 10.1016/j.fsi.2008.03.019

Reverter M, Bontemps N, Lecchini D, Banaigs B and Sasal P, 2014. Use of plant extracts in fish aquaculture as an alternative to chemotherapy: current status and future perspectives. Aquaculture, 433: 50-61, doi: 10.1016/j.aquaculture.2014.05.048

Reverter M, Tapissier Bontemps N, Sarter S, Sasal P and Caruso D, 2021. Moving towards more sustainable aquaculture practices: a meta analysis on the potential of plant enriched diets to improve fish growth, immunity and disease resistance. Rev Aquac, 13(1): 537-555, doi: 10.1111/raq.12485

Rico A and Van den Brink PJ, 2014. Probabilistic risk assessment of veterinary medicines applied to four major aquaculture species produced in Asia. Sci Total Environ, 468: 630-641, doi: 10.1016/j.scitotenv.2013.08.063

Ringø E, Olsen RE, Vecino JG, Wadsworth S and Song SK, 2012. Use of immunostimulants and nucleotides in aquaculture: A review. J Mar Sci Res Dev, 2(1): 104, doi: 10.4172/2155-9910.1000104

Sahu S, Das BK, Mishra BK, Pradhan J and Sarangi N, 2007. Effect of *Allium sativum* on the immunity and survival of *Labeo rohita* infected *with Aeromonas hydrophila*. J Applied Ichthyol, 23(1): 80-86, doi: 10.1111/j.1439-0426.2006.00785x

Scavo A, Rial C, Varela RM, Molinillo JMG, Mauromicale G *et al.*, 2019. Influence of genotype and harvest time on the *Cynara cardunculus* L. sesquiterpene lactone profile. J Agric Food Chem, 67(23): 6487-6496, doi: 10.1021/acs.jafc.9b02313

Secombes CJ, Bird S and Zou J, 2005. Adaptive immunity in teleosts: cellular immunity. Dev Biol, 121: 25-32

Selvaraj V, Sampath K and Sekar V, 2005. Administration of yeast glucan enhances survival and some non-specific and specific immune parameters in carp (*Cyprinus carpio*) infected with *Aeromonas hydrophila*. Fish Shellfish Immunol, 19(4): 293-306, doi: 10.1016/j.fsi.2005.01.001

Semwal A, Kumar A and Kumar N, 2023. A review on pathogenicity of *Aeromonas hydrophila* and their mitigation through medicinal herbs in aquaculture. Heliyon, 9(3): e14088, doi: 10.1016/j.heliyon.2023.e14088

Sharma A, Deo AD, Riteshkumar ST, Chanu TI and Das A, 2010. Effect of *Withania somnifera* (L. Dunal) root as a feed additive on immunological parameters and disease resistance to *Aeromonas hydrophila* in *Labeo rohita* (Hamilton) fingerlings. Fish Shellfish Immunol, 29(3): 508-512, doi: 10.1016/j.fsi.2010.05.005

Shirazi M, 2018. In vivo biological investigation of methanolic extract of *Thymus linearis* whole plant. Am J Ethnomed, 5(1-2): 1-5, doi: 10.21767/2348-9502.10002

Silva NCC and Fernandes Júnior AJJOVA, 2010. Biological properties of medicinal plants: a review of their antimicrobial activity. J Venom Anim Toxins Trop Dis, 16, 402-413, doi: 10.1590/S1678-91992010000300006

Steverding D, Morgan E, Tkaczynski P, Walder F and Tinsley R, 2005. Effect of Australian tea tree oil on *Gyrodactylus* spp. infection of the three-spined stickleback *Gasterosteus aculeatus*. Dis Aquatic Organisms, 66(1): 29-32, doi: 10.3354/dao066029

Stratev D, Zhelyazkov G, Noundou XS and Krause RW, 2018. Beneficial effects of medicinal plants in fish diseases. Aquac Int, 26: 289-308, doi: 10.1007/s10499-017-0219-x

Suzuki K, Misaka N, and Sakai DK, 2006. Efficacy of green tea extract on removal of the ectoparasitic flagellate *Ichthyobodo necator* from chum salmon, *Oncorhynchus keta*, and masu salmon, *O. masou*. Aquaculture, 259 (1-4): 17-27, doi: 10.1016/j.aquaculture.2006.05.004

Tadese DA, Sun C, Liu B, Muritu RW, Kevin NT *et al.*, 2020. Combined effects of emodin and *Clostridium butyricum* on growth and non-specific immunity of giant freshwater prawns, *Macrobrachium rosenbergii*. Aquaculture, 525: 735281, doi: 10.1016/j.aquaculture.2020.735281

Uribe C, Folch H, Enríquez R and Moran GJ VM, 2011. Innate and adaptive immunity in teleost fish: A review. Vet med, 56(10): 486-503, doi: 10.17221/3294-VETMED

Vallejos-Vidal E, Reyes-López F, Teles M and MacKenzie S, 2016. The response of fish to immunostimulant diets. Fish Shellfish Immunol, 56: 34-69, doi: 10.1016/j.fsi.2016.06.028

Van Doan H, Lumsangkul C, Hoseinifar SH, Harikrishnan R, Balasundaram C *et al*., 2021. Effects of coffee silverskin on growth performance, immune response, and disease resistance of Nile tilapia culture under biofloc system. Aquaculture, 543, 736995, doi: 10.1016/j.aquaculture.2021.736995

Van Hai N, 2015. The use of medicinal plants as immunostimulants in aquaculture: A review. Aquaculture, 446: 88-96, doi: 10.1016/j.aquaculture.2015.03.014

Varijakzhan D, Chong CM, Abushelaibi A, Lai KS and Lim SHE, 2020. Middle Eastern plant extracts: An alternative to modern medicine problems. Molecules, 25(5): 1126, doi: 10.3390/molecules25051126

Watts JE, Schreier HJ, Lanska L and Hale MS, 2017. The rising tide of antimicrobial resistance in aquaculture: sources, sinks and solutions. Marine Drugs, 15(6): 158, doi: 10.3390/md15060158

Wu CC, Liu CH, Chang YP and Hsieh SL, 2010. Effects of hot-water extract of *Toona sinensis* on immune response and resistance to *Aeromonas hydrophila* in *Oreochromis mossambicus*. Fish Shellfish Immunol, 29(2): 258-263, doi: 10.1016/j.fsi.2010.04.021

Xia YT, Cheng EH C, Wang HY, Zhang LHL, Lin SY *et al*., 2023. The extract from aerial part of *Scutellaria baicalensis* regulates gut microbiota in rabbit fish: replacement of antibiotic fighting against pathogenic bacteria. Aquaculture, 565, 739140, doi: 10.1016/j.aquaculture.2022.739140t

Zhu F, 2020. A review on the application of herbal medicines in the disease control of aquatic animals. Aquaculture, 526: 735422, doi: 10.1016/j.aquaculture.2020.735422

Received - 07.02.2025, Accepted - 24.05.2025, Published - 26.05.2025 (Online), 01.06.2025 (Print)
Section Editor: Dr. D. Kamilya, Editorial Board Member