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APPLICATIONS OF ANTIMICROBIAL PEPTIDES (AMPS) AS AN ALTERNATIVE TO ANTIBIOTIC USE IN AQUACULTURE – A MINI-REVIEW

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Abstract

The use of antibiotics for the control of infections has not only been banned by FDA for use in food-producing animals, but also several countries have prohibited their use in aquaculture because of several reasons such as the occurrence of antibiotic-tolerant microorganisms, accumulation of antibiotic residues in fish and shrimp flesh, and aquatic environmental effluence concerns. These issues have led researchers and aquaculture scientists to conduct several studies to find antibiotic alternatives. Numerous substitutes have been evaluated, such as probiotics, synbiotics, prebiotics, postbiotics, phytogenics, essential oils, and several others. Results show that these supplements demonstrate proven efficacy in enhancing immune responses, reducing mortalities resulting from experimental infections, and reducing antibiotic usage in medicated aquafeed. Nonetheless, using antimicrobial peptides (AMPs) to control fish diseases and as antibiotic alternatives is a promising and interesting research topic. AMPs are a vital class of small peptides that could stimulate the innate immune system against challenging pathogens and also possess significant potent defensive responses against a variety of infectious and non-infectious pathogenic agents, including bacteria, parasites, fungi, and viruses. Regarding their source origin, AMPs can be classified into six main types: mammalian-, amphibian-, insect-, aquatic-, plant-, and microorganism-derived AMPs. On account of their unique structure, they can display an essential function in therapeutic strategies against infectious diseases affecting fish and shrimp. Reports showed several kinds of AMPs had a wide spectrum of antimicrobial properties. These effects are besides their prominent immunostimulatory functions. Thus, they may be considered a functional alternative to antibiotics in aquaculture. This article provides information on the current knowledge about the modes of action, sources, classification, functions, and potential applications for the development of aquatic animal health. The information included in this context will be valuable to enhance the sustainability of aquaculture.

Key words: antimicrobial peptides (AMPs), antimicrobial, antiviral, antiparasitic, antifungal, aquaculture, antibiotic resistance

Fish pathogens, particularly bacterial ones, are an important category that causes devastating diseases and high economic loss to the infected fish (Austin and Austin, 2007; Abdel-Latif et al., 2020; El-Son et al., 2021; Korzekwa et al., 2022). These diseases are commonly treated with antibiotics (Assefa and Abunna, 2018; Naiel et al., 2020). However, the use of antibiotics has been prohibited and constrained in several countries throughout the globe (Naiel et al., 2021 a; Abdel-Latif et al., 2022 a; Yilmaz et al., 2022) because of several reasons, such as their accumulation in fish tissues and consequently affecting human health, development of antibiotic-resistant strains, and environmental concerns (Preena et al., 2020; Naiel et al., 2021 b). An ample number of research reports have been conducted to find harmless, cost-effective, and environmentally safe supplements and strategies to enhance immunity with the possible ability to replace antibiotic uses in aquaculture (El-Saadony et al., 2021; Abdel-Latif et al., 2022 b, c). Antimicrobial peptides (AMPs) play crucial roles in controlling pathogenic agents (Valero et al., 2020) and enhancing immunity and defense responses, with a well-known ability to be used as alternatives for antibiotic use in aquaculture (Tassanakajon et al., 2018; Rima et al., 2021). Current research studies that focused on using AMPs in aquaculture predominantly concentrated on their functions to build up competent immunity (Tassanakajon et al., 2018), augmenting the phagocytic activities and the digestion of the invading pathogens (D'Este et al., 2016; Naiel et al., 2022 a). AMPs also demonstrated a wide-spectrum activity in the face of a variety of pathogenic agents (Muncaster et al., 2018; Huan et al., 2020). Recent reviews showed that these compounds might also help decrease the problem of antimicrobial resistance in aquaculture (Lu et al., 2022; Naiel et al., 2022 b).

AMPs are promising antimicrobial and anti-infective compounds (Büyükkiraz and Kesmen, 2022). They are a class of small peptides (less than 13 kDa), having both

hydrophilic and hydrophobic parts and cationic charge. These molecules are vital constituents because they can promote the immune system and enhance the defensive responses against various pathogenic microbial agents (Ravichandran et al., 2010). AMPs could be identified from various organisms such as insects, plants, animals, and humans (Hancock, 2001) and also from aquatic origin (such as crustaceans, shrimp, fish, and several aquatic organisms) (Huan et al., 2020). Fish-derived AMPs are produced in the skin epidermis layer and gill filaments and are considered the most important defensive line against challenging pathogens (Lieke et al., 2020).

It was found that more than 5,500 AMPs have been discovered, isolated, identified, and characterized (Zhao et al., 2013). However, they display variations in their structures; they have common properties such as cationic charge and amphipathic and hydrophobic structures (Hancock and Lehrer, 1998; Hancock and Rozek, 2002). AMPs have a positive charge from nearly 20 to 50 amino acid sequences and have some essential amino acids such as arginine and lysine (Hancock, 2001). Because of disulfide bridges present in the AMPs structure, they are responsible for the positive charge and hydrophilic features (Hancock, 2001). The structural variations of cationic AMPs are responsible for the high antimicrobial activities of these important molecules (Vanhoye et al., 2003). Numerous AMPs have been characterized, such as defensins, paenicidins, hepicidins, cathelicidins, and several others (Cederlund et al., 2011).

These molecules also showed immunomodulatory effects against infectious diseases (Mayer et al., 2010; Steinstraesser et al., 2011; Negm et al., 2021). In this review article, we will go in-depth to discuss the modes of action of AMPs. In addition, recent studies on the resources of AMPs and their importance as antibacterial, antiviral, antiparasitic, and antifungal effects will also be elucidated. The advantages and limitations of using these molecules will also be assessed. The information included in this review article will be interesting for improving aquatic animal health and enhancing the sustainability of aquaculture.

Classification of AMPs

● Classification of AMPs according to their peptide structure

AMPs could be categorized into four main categories (as shown in Figure 1) on the basis of their peptide structures, including 1) α-helical AMPs, 2) β-sheet AMPs, 3) linear extended structure AMPs, and 4) mixed AMPs (Huan et al., 2020).

The α-helical AMPs

The α-helical AMPs include several molecules as cecropins, magainins and pleurocidins, chrysophins, piscidins, moronecidins, misgurnin, pardaxin, and cathelicidins, and they are isolated from insects, amphibian, or teleost fish (Park et al., 1997; Douglas et al., 2001; Lauth et al., 2002; Iijima et al., 2003; Chang et al., 2006; Silphaduang et al., 2006). They are rarely found in invertebrates, although styelins, dicynthaurin, halocidin, clavanins and clavaspirin were detected in tunicate hemocytes (Lee et al., 1997 a, b).

The β-sheet AMPs

The β-sheet AMPs include amino acids combined with disulfide peptides as defensins, mytilins, tachyplesins, polyphemusins, myticins, hepcidins, and mytimycins (Saito et al., 1995; Charlet et al., 1996; Mitta et al., 2000; Yang et al., 2007; Cho et al., 2009).

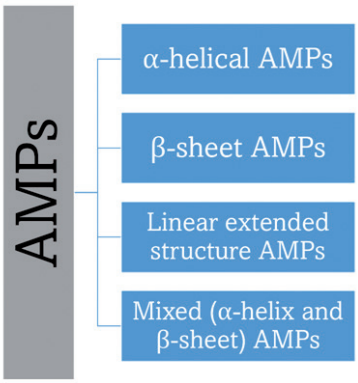

Figure 1. Classification of antimicrobial peptides (AMPs) according to their peptide structure

Extended linear structure AMPs

They are linear extended structure peptides and comprise high amino acid contents as histidine, proline, tryptophan, and arginine. Their antimicrobial effects could be attributed to their ability to interact with intracellular proteins, such as heat shock protein (HSP) (Nayab et al., 2022).

Mixed AMPs

This class of AMPs consists of α-helix and β-sheet AMPs and contains abundant levels of proline and arginine (Nayab et al., 2022).

● Classification of AMPs according to the amino acid-rich species

AMPs could also be classified in accordance with the amino acid-rich types (as presented in Figure 2) into five classes known as proline-, tryptophan-, arginine-, histidine-, and glycine-rich AMPs. Details on these classes have been described by Huan et al. (2020).

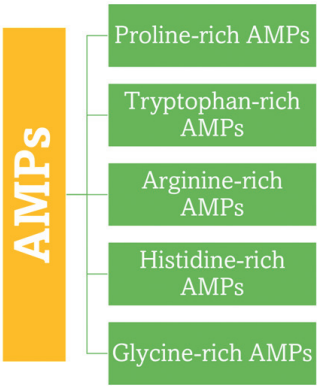

Figure 2. Classification of antimicrobial peptides (AMPs) according to amino acid-rich species

● Classification of AMPs according to their source origins

AMPs could also be classified according to their source origins (as depicted in Figure 3) into six classes known as a) mammalian AMPs, b) amphibian-derived AMPs, c) insect-derived AMPs, d) microorganism-derived AMPs, e) aquatic-derived AMPs, and f) plant-derived AMPs.

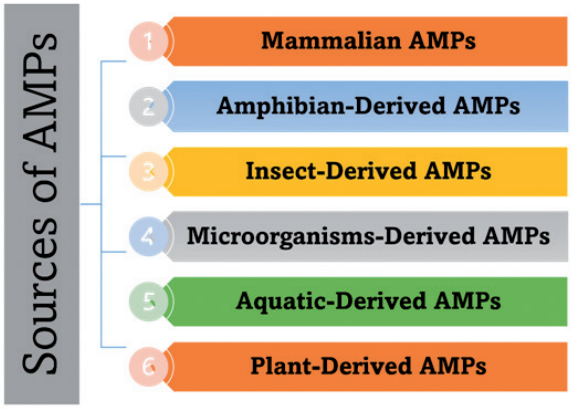

Figure 3. Types of antimicrobial peptides (AMPs) according to their source origins

Mammalian AMPs

These AMPs are discovered in human beings, cattle, sheep, and other vertebrates. They contain 2 main classes known as cathelicidins and defensins (Reddy et al., 2004).

Amphibian-derived AMPs

These AMPs are isolated from amphibians, particularly frogs. They play a vital role in protecting amphibians against challenging pathogens (Rollins-Smith, 2009).

Insect-derived AMPs

These AMPs are mainly produced in insect bodies, and their functions mainly focus on increasing insect survivability (Vilcinskas, 2013). An ample number of insects can produce several insect-derived AMPs, such as guppy silkworm, *Drosophila*, and black soldier fly (*Hermetia illucens*) (Abdel-Tawwab et al., 2020).

Microorganism-derived AMPs

These AMPs can be acquired from several microorganisms as fungi and bacteria, such as *Lactococcus lactis*, *Bacillus brevis,* and *B. subtilis* (Huan et al., 2020).

Plant-derived AMPs

These AMPs are the main component of the defense system of several plants. They have been characterized and defined from diverse plant parts, especially seeds, roots, flowers, leaves, and stems from various plants such as cereals, legumes, fruits, and vegetables. These molecules can protect plants in the face of numerous pathogens (Nawrot et al., 2014; Sharma et al., 2022). An example of plant-derived AMPs is cyclotide, which has been isolated from *Bauhinia rufescens* leaves with proven antibacterial efficacy against fish pathogens (Nganso et al., 2020).

Aquatic-derived AMPs

These AMPs can be isolated from a variety of aquatic organisms such as fish (Valero et al., 2020), crabs (Brockton and Smith, 2008; Marggraf et al., 2018), shrimp (Hu et al., 2006), mussels (Roch et al., 2008), and others (Silva et al., 2015). These molecules possess immunomodulatory functions and antimicrobial effects against several pathogens.

AMPs mechanisms of action

The possible mechanisms of AMPs could be illustrated in several points, as depicted in Figure 4. Three suggested modes of action are as follows: a) their immunostimulatory functions, b) membrane-active mechanisms, and c) non-membrane active mechanisms.

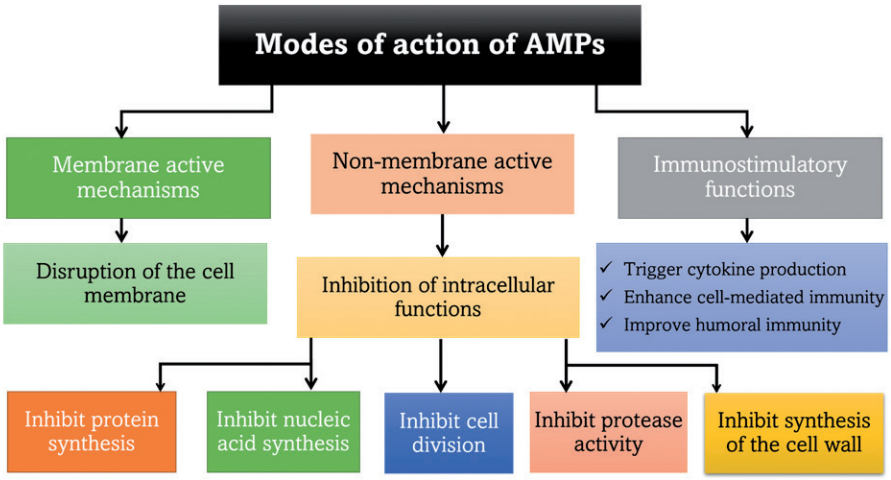

Figure 4. Hypothesized mechanisms of action of antimicrobial peptides (AMPs) in accordance with the published literature

Table 1. Types and potential antimicrobial activities of some selected antimicrobial peptides (AMPs) derived from different sources against the most common infectious fish pathogens according to the published literature

AMPs classes	Types	AMPs	Sources	Activities	Infectious fish pathogens	References
1	2	3	4	5	6	7
1. Fish-derived AMPs	Chionodracine	Piscidin-like AMPs	Antarctic icefish (*Chionodraco hamatus*)	Antibacterial	*E. coli* *Psychrobacter* spp.	(Buonocore et al., 2012)
	NK-Lysin	Saposin-like protein AMPs	Large yellow croaker (*Larimichthys crocea*)	Antibacterial	*Staphylococcus aureus* *E. coli* *Vibrio harveyi* *Vibrio parahaemolyticus* *Aeromonas hydrophila* *Photobacteria damselae*	(Zhou et al., 2016)
	Piscidin	Cationic AMPs	Rock bream (*Oplegnathus fasciatus*)	Antibacterial	*Streptococcus iniae* *Vibrio harveyi* *Vibrio campbellii* *Vibrio alginolyticus* *Vibrio ordalii* *Vibrio vulnificus* *Edwardsiella tarda* *E. coli*	(Bae et al., 2016; Umasuthan et al., 2016)
	Moronecidin	Cationic AMPs	Hybrid striped bass (*Morone saxatilis* × *M. chrysops*)	Antibacterial	*Enterococcus faecalis* *Vibrio cholerae* *E. coli*	(Lauth et al., 2002)
	Chrysophsin	Cationic AMPs	Red seabream (*Chrysophrys major*)	Antibacterial	*Lactococcus garvieae* *Streptococcus iniae* *Vibrio anguillarum* *Vibrio penaeicida* *Vibrio harveyi* *Aeromonas salmonicida* *Enterococcus faecalis* *E. coli* *Vibrio vulnificus* *Pseudomonas putida*	(Iijima et al., 2003)
	Histone-like proteins (HLPs)	Bacterial DNA binding protein	Channel catfish (*Ictalurus punctatus*)	Antibacterial	*Vibrio alginolyticus* *Aeromonas hydrophila* *E. coli*	(Robinette et al., 1998)
	β-defensin	Non-cationic AMPs	Japanese flounder (*Paralichthys olivaceus*)	Antibacterial	*E. coli*	(Nam et al., 2010)
	Hepcidin	Non-cationic AMPs	Orange-spotted grouper (*Epinephelus coioides*)	Antibacterial	*Vibrio vulnificus* *Staphylococcus aureus*	(Zhou et al., 2011)

Table 1 – contd.

1	2	3	4	5	6	7
2. Plant-derived AMPs	Cyclotide	Cysteine-rich AMP	*Bauhinia rufescens* leaves	Antibacterial	*E. coli* *Aeromonas salmonicida* *Flavobacterium psychrophilum* *Vibrio anguillarum* *Vibrio ordalii*	(Nganso et al., 2020)
3. Crustacean-derived AMPs	Penaeidin class 5	Penaeidins	Black tiger shrimp (*Penaeus monodon*)	Antifungal	*Fusarium pisi* *Fusarium oxysporum*	(Hu et al., 2006)
				Antibacterial	*Aerococcus viridans* *Vibrio alginolyticus*	
	Defensin	Cysteine-rich cationic AMP	The blue mussel (*Mytilus edulis*)	Antibacterial	*E. coli* *Aerococcus viridans* *Enterococcus faecalis* *Staphylococcus aureus*	(Charlet et al., 1996)
	Mytilin	Cysteine-rich cationic AMP	The Mediterranean mussel (*Mytilus galloprovincialis*)	Antibacterial	*Vibrio splendidus* *Vibrio anguillarum* *E. coli*	(Roch et al., 2008)
				Antiviral	*White spot syndrome virus*	
	Myticin C	Cysteine-rich cationic AMP	The Mediterranean mussel (*Mytilus galloprovincialis*)	Antibacterial	*Enterococcus faecalis* *Staphylococcus aureus* *E. coli*	(Domeneghetti et al., 2015)
	Mytimycin (MytM)	A cationic rich cysteine-AMP	The Mediterranean mussel (*Mytilus galloprovincialis*)	Antifungal	*Fusarium oxysporum*	(Sonthi et al., 2012)
	Penaeidins	Shrimp AMP	*Penaeus vannamei*	Antibacterial	*Some Vibrio species*	(Destoumieux et al., 2000)
	Carcinin	Crustin-type AMP	Common littoral crab (*Carcinus maenas*)	Antibacterial	*Planococcus citreus*	(Brockton and Smith, 2008)
	Polyphemusin III	A cationic β-hairpin AMP	Atlantic horseshoe crab (*Limulus polyphemus*)	Antibacterial	*E. coli* *Pseudomonas aeruginosa* *Staphylococcus aureus*	(Marggraf et al., 2018)
4. Aquatic-derived AMPs	Clavanin A	Alpha-helical AMP	Asian tunicate (*Styela clava*)	Antibacterial	*Staphylococcus aureus* *E. coli*	(Silva et al., 2015)
	Styelin	Phenylalanine-rich AMP	Asian tunicate (*Styela clava*)	Antibacterial	*E. coli* *Pseudomonas aeruginosa*	(Lee et al., 1997 a)

Membrane-active mechanisms

The membrane-active mechanism of AMPs is closely related to their ability to disrupt the cell membrane of bacteria, fungi, or other microorganisms (Huan et al., 2020). AMPs mechanism may depend on its cationic nature by allowing its binding capability to the negatively charged lipopolysaccharides that are present in the cell membrane of the invading pathogens through electrostatic forces. During this reaction, AMPs obtain an amphipathic conformation that enhances the binding ability towards the cell membrane of the challenging pathogen. This type of AMPs is defined as permeabilizing membrane AMP because of its potential to induce pores on the entire cell surface membrane following their electrostatic reaction, consequently performing in the discharge of cellular constituents and sudden cell death (Sengupta et al., 2008).

Non-membrane active mechanisms

These mechanisms depend on the inhibition of intracellular functions. They include several points (as illustrated in Figure 4) such as a) the inhibition of steps required for the biosynthesis of protein, such as transcription and translation (Mardirossian et al., 2014), b) the inhibition of nucleic acid biosynthesis, as they can inhibit some essential enzymes such as DNA topoisomerase I enzyme and therefore, enhance nucleic acid degradation process (Subbalakshmi and Sitaram, 1998), c) possess an important inhibitory effect on protease enzyme activities of several bacterial cells (Huan et al., 2020), and d) inhibition of the cellular division through inhibition of the DNA replication process (Lutkenhaus, 1990).

Advantages and limitations of the use of AMPs

AMPs have several benefits, such as their low synthesis cost, easy storage for a long time in relatively large quantities, and rapid availability after an infection (Ravichandran et al., 2010). Despite these advantages, AMPs may face some critical drawbacks and restrictions, such as their decreased stability at different pH ranges, their action in the disruption of the eukaryotic cell membrane may trigger several adverse hemolytic effects, and high technical and production cost restrictions of their industrial manufacture (Zhu, 2008; Oeemig et al., 2012; Semreen et al., 2018). Besides, the deficiency of data availability on their toxicological effects, pharmacodynamics, pharmacokinetics, and inactivity in the presence of some ions such as Ca^{2+}, Fe^{2+}, and other serum constituents (Thackray and Moir, 2003; Zhou et al., 2016). The potential efficacy of AMPs in light of the impacts of climate change on altering the acidity of the oceans may also need further investigation.

Benefits and applications of AMPs in aquatic animal medicine

According to the published literature, the benefits and applications of AMPs in aquaculture can be summarized in Figure 5.

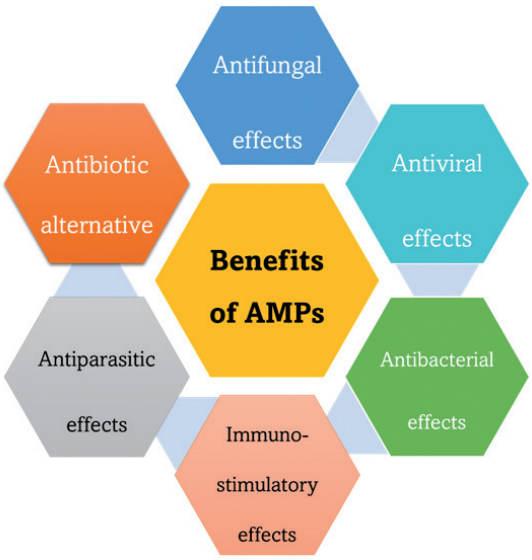

Figure 5. Benefits and potential applications of antimicrobial peptides (AMPs) in aquaculture according to the published literature

Antifungal activities of AMPs

Several fish-derived AMPs have shown significant antifungal activities against a variety of fungal species. For example, it was found that piscidin-2 identified from hybrid striped bass (*Morone saxatilis* × *M. chrysops*) showed proven fungicidal activity against *Malassezia furfur*, *Candida albicans*, and *Trichosporon beigelii* (Sung et al., 2008). Moreover, it was also found that the AMP "Ofpis-1" characterized from *Oplegnathus fasciatus* (Umasuthan et al., 2016), and the AMPs "Oreoch-1, Oreoch-2, and Oreoch-3" derived from *Oreochromis niloticus* (Acosta et al., 2014) demonstrated high antifungal efficiency against *C. albicans* and *Saccharomyces cerevisiae*. Zhuang et al. (2017) indicated that hepcidins (ecPis-2S, ecPis-3S, and ecPis-4S) isolated from *Epinephelus coioides* had powerful antifungal effects against *Pichia pastoris*. Furthermore, the synthetic hepcidin AMP derived from hybrid striped bass exhibited antifungal influence against *Aspergillus niger* (Lauth et al., 2005). Moreover, the AMP "AS-hepcidin-6" isolated from *Acanthopagrus schlegelii* had potent antifungal activity against *C. albicans* (Yang et al., 2011). Another hepcidin AMP known as "PChepc" isolated from *Pseudosciaena crocea* displayed antifungal activity against several fungus strains such as *Fusarium graminearum*, *C. albicans*, and *F. solani* (Wang et al., 2009). Of interest, 2 histone-like AMPs (HLP-1 and HLP-2) isolated from *Ictalurus punctatus* revealed proven antifungal activities against an important fish fungal pathogen known as *Saprolegnia parasitica* (Robinette et al., 1998). A similar function has also been performed by piscidin-2, as illustrated by Zahran and Noga (2010). Also, synthetic histone-like proteins performed synergistic antifungal effects against *Tetrahymena pyriformis* and *Saprolegia* spp. when combined with antifungal agents such as copper sulphate and malachite green (Zahran and Noga, 2010). Atlantic cod (*Gadus morhua*) could diminish *C. albicans*

infection by exerting mucus containing H2B AMP and three types of ribosomes-originated AMPs (L40, L35, and L36A) (Bergsson et al., 2005). Moreover, the AMP "parasin I" identified from *Parasilurus asotus* induced a high efficiency against *C. albicans*, *S. cerevisiae,* and *Cryptococcus neoformans* (Park et al., 1998). The antifungal activity of the AMP "myxinidin", which was isolated from hagfish (*Myxine glutinosa*), has been proven to have antifungal action against *C. albicans* (Subramanian et al., 2009). Similarly, the AMP "misgurin" characterized from the loach (*Misgurnus anguillicaudatus*) also exhibited antifungal activities against *C. albicans*, *C. neoformans,* and *S. cerevisiae* (Park et al., 1997). Furthermore, the AMP "epinecidin-1" defined from the orange-spotted grouper had high antifungal effects on *Cylindrocarpon* sp., *Trichophytonsis mentagrophytes*, and *Microsporosis canis* (Yin et al., 2006).

Anti-parasitic activity of AMPs

Parasitic infestation negatively affects the health status and economic returns of global finfish aquaculture production (Abdel-Latif and Khafaga, 2020). Fish parasites directly lead to high losses in fish production by decreasing final fish yield or indirectly by increasing the treatment costs (Woo, 1992; Noga, 2010). Regarding the antiparasitic activities of AMPs, Colorni et al. (2008) found that the synthetic AMP "piscidin-2" that derived from hybrid striped bass showed strong antiparasitic activities against a variety of fish ectoparasites such as the beautiful protozoan (*Trichodina* sp.), velvet-effect causing parasite (*Amyloodinium ocellatum*), and ciliated protozoans causing Ich disease known as *Cryptocaryon irritans* in marine fish and *Ichthyophthirius multifiliis* in freshwater fish. Moreover, it was also illustrated that the AMP "Ofpis-1" obtained from rock bream acquired proven antiparasitic activities against a unicellular marine eukaryote known as *Miamiensis avidus*, as illustrated by Umasuthan et al. (2016). In the same way, the cationic piscidin-1, the non-cationic piscidin-2, and the splicing variant piscidin-2b that originated from Atlantic cod displayed proven antiparasitic activities against a unicellular eukaryote free-living ciliate known as *Tetrahymena pyriformis* (Ruangsri et al., 2012). Likewise, the synthetic AMP "ecPis-3" identified from orange-spotted grouper can disrupt the membrane of the infective stage of *C. irritants* (Zhuang et al., 2017). Attractively, the AMP "HLP-1" characterized from hybrid striped bass demonstrated potent antiparasitic effects against *A. ocellatum* trophonts (Noga et al., 2002). The AMP "HbβP-1" defined from *I. punctatus* also demonstrated antiparasitic effects against trophont stages of Ich-disease-causing parasites and *T. pyriformis* (Ullal et al., 2008).

The antiviral activities of AMPs

Several AMPs isolated from fish have been proven to have antiviral properties. For example, Chinchar et al. (2004) declared that the AMPs "piscidin-1N, piscidin-1H, piscidin-1 and piscidin-2" identified and characterized from hybrid striped bass showed higher efficiency against channel catfish virus. Also, beta-defensin 2 (zfBD2) isolated from zebrafish induced significant decrease of spring viremia of carp virus infection in both *in vitro* and *in vivo* studies (García-Valtanen et al., 2014). The AMP "β-defensin" defined from orange-spotted grouper liver showed a potential ability to diminish the pathogenicity of Singapore grouper iridovirus and nervous necrosis virus (Guo et al., 2012). Furthermore, the AMP "β-defensin" obtained from orange-spotted grouper testis and pituitary gland proved higher effectiveness towards RGV iridovirus (Jin et al., 2010). Additionally, the synthetic spotted scat (*Scatophagus argus*) hepcidin, SA-hepcidin-1 or SA-hepcidin-2, seems to be active against *Siniperca chuatsi* rhabdovirus and largemouth bass *Micropterus salmoides* reovirus, using the epithelioma papulosum cyprini, and the SA-hepcidin-2 revealed the higher antiviral activity (Gui et al., 2016). The AMP "CsNKL1-derived synthetic peptide NKLP27" exhibited proven antiviral effects against megalocytivirus RBIV-C1 (Zhang et al., 2014). Despite the antiviral activity of many fish-derived AMPs, the entire cellular mechanisms are still unclear and warrant additional further investigations.

The antibacterial activity of AMPs

Several studies had investigated the antibacterial activities of several AMPs. For instance, Gyan et al. (2020) declared that fortified Pacific white-leg shrimp diets with 0.4% AMPs significantly promoted growth, serum antioxidant status, and innate immunity and reduced the mortality rate induced by *Vibrio harveyi* infection. Likewise, the liver-expressed AMP-2 (LEAP-2) isolated from *Trachinotus ovatus* significantly inhibited the *Edwardseilla tarda* and *Streptococcus agalactiae* and stimulated the immunity and defense against infections in the same fish species (Lei et al., 2020). At the same trend, Xie et al. (2020) found that the chemically synthesized Spgly-AMP peptides from *Scylla paramamosain* displayed high antibacterial effects against an ample number of G+ve and G-ve bacterial strains. Besides, Shan et al. (2020) declared that the AMP "NKL-24" derived from zebrafish NK-lysin could kill *Vibrio parahaemolyticus* and enhance a non-specific immunity of Yesso scallop (*Patinopecten yessoensis*).

Possibility of use of AMPs as antibiotic alternatives

AMPs comprise important compounds with known and proven antibacterial, antifungal, antiviral, and antiparasitic activities against a wide range of fish-associated pathogens, including bacteria, fungi, viruses, and parasites (Brogden, 2005). A number of benefits were noticed for the use of AMPs over the use of traditional antibiotics. For instance, (a) the commonly found resistance mechanisms against the conventionally used antibiotics are avoided by the use of AMPs (Wang et al., 2016), (b) AMPs are simpler to be synthesized as they are usually comprised of short sequences of several amino acids

(Hansen et al., 2020), (c) AMPs show rapid killing abilities (Raheem and Straus, 2019), (d) AMPs can induce their actions against bacterial strains regardless of their phenotype of resistance as they are not influenced by the established antibiotic-resistance mechanisms (Park et al., 2011; Lee et al., 2020), and (e) these molecules do not also influence the gut-associated microbial communities, which is often affected by the conventionally and traditionally used antibiotics (Kim et al., 2020). These benefits may enhance the possibility of numerous AMPs being used as antibiotic alternatives in medicated feed (Rima et al., 2021). However, these ideas are still a hotspot of ongoing studies and merit further investigations. Comprehensive *in vivo* and *in vitro* studies should also be conducted to make a comparison between the effects of AMPs and several traditional antibiotics for controlling bacterial infections affecting fish and shrimp. The results and findings of these comparisons should concentrate on several important issues, including the development of resistant strains, environmental concerns, and safety margins for aquatic organisms and human beings.

Concluding remarks and future perspectives

Fish and shrimp are always subjected to various pathogenic agents from their surrounding environment, causing high mortality and economic losses. Antibiotics are crucial in controlling infections, decreasing mortalities, and supporting general health status. However, the wide application of antibiotics in farms has increased antibiotic-resistant bacterial strains and several other drawbacks. The scientists focus on developing a new applicable strategy to control infections with minimal negative adverse effects on fish, humans, and aquatic environments. AMPs have gained great attention as immunostimulatory molecules that stimulate the immune defense against infectious diseases with well-known abilities to inhibit several infections, such as fungi, viruses, parasites, and bacteria. These functions make the AMPs as functional promising candidates and effective molecules against infectious diseases with several advantages over the traditionally used antibiotics. Several research limitations are still present in this topic, such as the efficacy and applicability of AMPs under field trials. Moreover, the antifungal, antiviral, and antiparasitic effects of AMPs also need several *in vivo* and *in vitro* trials to understand their precise modes of action better. All the aforementioned points and several others necessitate more and more investigations to stand on solid ground when discussing the potential uses of these important molecules in the field of aquaculture.

Declaration of competing interest

None.

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