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Chemical aspects of the preservation and safety control of sea foods

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Abstract: The interest in biopreservation of food has prompted the quest for new natural antimicrobial compounds from different origins. Antimicrobial peptides (AMPs) are found widely distributed through nature, and participate in the innate host defense of each species. Fish are a great source of these peptides and fish-derived peptides exhibit broad-spectrum antimicrobial activity. This review introduces the general characteristics and biological activity of fish-derived AMPs, discusses the gene engineering of fish-derived AMPs and antibacterial mechanism, and emphasizes the importance of novel biopreservation strategies and their application to ensure aquatic products quality and safety.

***Keywords*:** Fish-derived peptides; Antibacterial; Mechanism; Quality safety

1. Introduction

There is a growing concern that the use of chemical synthetic preservatives in food industry may cause various potential hazards to human being health. Thus, safe natural food preservatives have become the priority in food industry to improve the safety of food products for decades. The application of antimicrobial peptides (AMPs) without toxic or other adverse effects has received great attention. Antimicrobial peptides represent a broad category of different families of highly conserved peptides widely found throughout the world, which show broad-spectrum antimicrobial effect on bacterial, viral, fungal, and other pathogens [1]. AMPs have been discovered at least 30 years [2], and the first AMP reported in teleosts dated back at 1986 [3-4]. The research on AMPs have attracted and fascinated scientists since then [5-6], and still AMPs related research is a hot topic on food and life sciences [7-8]. Fish possess a strong innate immune system, which acts as the first line of defense against pathogen infections. In general, fish-derived AMPs

are secreted in the mucus, saliva, circulatory system, and other parts which are high-risk pathogen targets [9-10]. Some results of research demonstrated that fish-derived AMPs exhibit many characteristics as other vertebrate AMPs, like broad-spectrum antimicrobial activities, as well as immunomodulatory functions. In addition, there seem to be interesting difference, specific to fish, that have evolved to show the unique aquatic environments and microbes encountered by these species [1]. Since information on the structure, molecular functions, and mechanisms is extensively available, this review focuses on AMPs reported in fish and their prospective applications promising strategies for quality and safety of aquatic products.

In this review, we introduce the general characteristics and biological activity of fish-derived AMPs. Additionally, we discuss the gene engineering of AMPs and antibacterial mechanism. In addition, the applications of fish AMPs on antimicrobial function for quality and safety of aquatic products are also mentioned.

2. The general characteristics and biological activity of AMPs

Recently, more attention has been focused on the identification and characterization of the composition, structure and, sequences of fish-derived AMPs [11]. These peptides generally contain 2–50 amino acid units. The amino acid composition and sequences can affect the activity of AMPs. According to their different structure characteristics, the AMPs of fish can be divided into three categories (Table 1): linear amphipathic α-helix peptides, cysteine-rich peptides and histone-like peptides.

2.1 Linear amphipathic α-helix

The antibacterial peptide generally has strong cationic properties, and can be folded into a hydrophobic or amphipathic alpha helical structure, which is conducive to the

bacterial cell membrane penetration. The first α-helix structure AMP isolated and characterized from skin mucous secretions of the winter flounder, *Pleuronectes americanus*, called pleurocidin, which was a 25-residue peptide [12]. Concomitantly, a family of peptides was characterized in the loach (*Oriental weatherfish*), *Misgurunus anguillicaudatus*, named misgurin [13]. A similarly α-helix structured peptide, called piscidins, was obtained in the mast cells of the hybrid striped bass [14]. Other similar peptides, including Myxinidin, epinecidin-1, moronecidin, pardaxin and dicentracin have been identified [15-20]. Linear amphipathic α-helix peptides are common active against Gram-positive and Gram-negative bacteria.

2.2 cysteine-rich peptides

Fish-derived cysteine-rich peptides, containing β-sheets and disulphide bonds, mainly contain cathelicidins, defensins and hepcidin. Cathelicidins have been discovered in species including *Oncorhynchus mykiss*, *Salmo sala* and *Gadus morhua* [21]. They share the common features of mammalian cathelicidins, such as four invariant cysteines clustered in the C-terminal region of the cathelin-like domain [22]. Both cathelicidins have four cysteine residues in C-terminal and contain two disulfide bonds. Many species of bony fish also carry defensins, these defensins generally contain six conservative cysteines, 3 β-fold lamellar structure, one more helical structure than mammals and birds. Defensins not only have antibacterial functions, but also have antiviral activities. According to some reports, defensins can inhibit the HIV-1, adenovirus, influenza virus, parainfluenza virus 3 (PIV-3), respiratory syncytial virus (RSV), vaccinia virus (VV), herpes simplex virus and Chandipura virus [23].

2.3 histone-like peptides

Histones are small, abundant basic proteins, which are most commonly found in association with DNA in the chromatin of eukaryotes [24]. Four histones, H2A, H2B, H3 and H4 are important for chromosome organization in the nucleosome. Some studies have suggested that histones have additional functions, including hormone activity and activation of leucocytes in salmon [25-26]. Park et al obtained an antimicrobial peptide in the skin mucous extracts of the injured catfish at 1998, and research showed that catfish produced the peptide named parasin I from histone H2A to protect against the invasion of microorganisms [27]. The complete amino acid sequence of parasin I was Lys-Gly-Arg-Gly-Lys-Gln-Gly-Gly-Lys-Val-Arg-Ala-Lys-Ala-Lys-Thr-Arg-Ser-Ser, and the Amino acid sequence homology analysis showed that parasin I was highly homologous to the N-terminal region of histone H2A. Parasin I had a molecular mass of 2000.4 Da and consisted of 19 amino acids, including five lysines and three arginines, which contributed to the net charge of +8. Richard et al separated a new peptide from Atlantic salmon, its amino acid sequence was similar to Histone H1, and the MIC of this peptide on *E.coli* was 31μg/ml [28]. Birkemo et al isolated and identified hipposin from Atlantic halibut skin secretion [29]. Amino acid sequence analysis showed that about 50 amino acids was highly homologous to the N-terminal region of histone H2A, and hipposin was active against both Gram-positive and Gram-negative bacteria.

Table 1 List of fish source AMPs.

Category	AMP	Source	Amino acid sequence	G^+	G^-	Fungi	virus	hemolysis	Ref.
α-helix	Chrysophsin-1	Red sea bream (*Chrysophrys major*)	FFGWLIKGAIHAGKAIHG LIHRRRH (25)	+	+			+	[30]
	Chrysophsin-2	Red sea bream (*C. major*)	FFGWLIRGAIHAGKAIHG LIHRRRH (25)	+	+			+	[30]
	Chrysophsin-3	Red sea bream (*C. major*)	FIGLLISAGKAIHDLIRRRH (20)	+	+			+	[30]
	Moronecidin	Striped bass (*Morone saxatilis*×*M. chrysops*)	FFHHIFRGIVHVGKTIH(K/R)LVTGT (22)	+	+	+		+	[31-32]
	Pleurocidin	Winter flounder (*Pleuronectes americanus*)	GWGSFFKKAAHVGKHVG KAALTHYL (25)	+	+			−	[33]
	Piscidin-1	Striped bass (*Morone saxatilis*)	FFHHIFRGIVHVGKTIHRL VTG (22)	+	+	+		+	[34-35]
	Piscidin-3	Striped bass (*Morone saxatilis*)	FIHHIFRGIVHAGRSIGRFL TG (22)	+	+			+	[34-35]

	Epinecidin-1	Grouper (*Epinephelus coioides*)	GFIFHIIKGLFHAGKMIHGLV (21)	+	+	+	[17]
	Misgurin	Mudfish (*Misgurnus anguillicaudatus*)	RQRVEELSKFSKKGAAARRRK (21)	+	+	−	[13]
	Dicentracin	European bass (*Dicentrarchus labrax*)	FFHHIFRGIVHVGKSIHKLVTG (22)				[16]
	Piscidin-2	Striped bass (*Morone saxatilis*)	FFHHIFRGIVHVGKTIHKLVTG (22)	+	+	+	[35]
	Hepcidin	hybrid striped bass	GCRFCCNCCPNMSGCGVCCRF	+			[36]
	Hepcidin	Medaka (*Oryzias latipes*)	QSHISMCTMCCNCCKWYKGCGFCCRF (26)				[18]
	Hepcidin	Red sea bream (*Chrysophrys major*)	RCRFCCRCCPRMRGCGLCCQRR (22)		+		[18]
cysteine-rich	Hepcidin	Striped bass (*Morone saxatilis*×*M. chrysops*)	HSSPGGCRFCCNCCPNMSGCGVCCPF (26)				[18]
	Hepcidin	Trout (*Oncorhynchus mykiss*)	SHLSLCRWCCNCCHNKGGFCCKF (23)				[18]
	Hepcidin	Turbot (*Scophthalmus maximus*)	QSHISLCRWCCNCCKANKGCGFCCKF (26)	+	+		[12]

Hepcidin	Zebrafish (*Danio rerio*)	LCRFCCKCCRNKGCGYC CKF (20)	+	+			[36]
JF-1(hecipin)	Japanese flounder (*Paralichthys olivaceus*)	DVKCGFCCKDGGCGVCC NF (19)	+	+		−	[38]
JF-2(hecipin)	Japanese flounder (*P. olivaceus*)	HISHISMCRWCCNCCKAK GCGPCCKF (26)	+	+		−	[38]
TH1-5(hecipin)	Tilapia (*Oreochromis mossambicus*)	GIKCRFCCGCCTPGICGVC CRF (22)	+	+			[39]
TH2-3(hecipin)	Tilapia (*O. mossambicus*)	QSHLSLCRWCCNCCRSN KGC (20)	+	+			[39]
fuBD1(β-Defensin)	Fugu (*Takifugu rubripes*)	ASFPWTLPSLSGVCRKVC LPTEMFFGPLGCGKGFQC CVSHFL (42)			+		[23]
ogBD1(β-Defensin)	Orange spotted grouper (*Epinephelus coioides*)	NDPEMQYWTCGYRGLCR RFCHAQEYIVGHHGCPRR YRCCAVRS (43)			+		[23]
omBD1(β-Defensin)	Rainbow trout (*Oncorhynchus mykiss*)	ASFPFSCPTLSGVCRKLCL TEMFFGPLGCGKGFLCCV SHF (40)			+		[23]

tnBD1(β-Defensin)	Pufferfish (*Tetraodon nigroviridis*)	ASFPWACPSLNGVCRKVC LPTELFFGPLGCGKGFLCC VSHFL (42)			+		[23]
tnBD2(β-Defensin)	Pufferfish (*T. nigroviridis*)	EDSDSEMQYWTCGYRGL CRRFCYAQEYTVGHHGC PRRYRCCATRP (45)			+		[23]
oncorhyncin III	Rainbow trout (*Oncorhynchus mykiss*)	6671 Da partial N-terminal sequence PKRKSATKGDEPA	+	+		−	[40]
Oncorhyncin III	Rainbow trout (*O. mykiss*)	Sequence not available (66)	+	+		+	[40]
Cathelicidin	Arctic char (*Salvelinus alpines*)	RRSRSGRGSGKGRGGSRG SSGSRGSKGPSGSRGSSGS RGSKGSRGGRSGRGSTIA GNGNRNNGGTRTA (68)		+			[41]
Cathelicidin	Atlantic cod (*Gadus morhua*)	SRSGRGSGKGGRGGSRGS SGSRGSKGPSGSRGSSGSR GSKGSRGGRSGRGSTIAG NGNRNNGGTRTA (67)		+			[42-43]
Cathelicidin	Brown trout (*Salmo truttafario*)	RRSQARKCSRGNGGGIRC PGGGIRL (26)					[44]
Cathelicidin	Grayling (*Thymallus thymallus*)	RRSKSSSNGGRKGSKGGS KG (20)					[44]
AsCath-1 (Cathelicidin)	Atlantic salmon (*Salmo salar*)	RRGKPSGGSRGSKMGSK DSKGGWRGRPGSGSRPGF GSSI (39)	+	+			[2]

AsCath-2(Cathelicidin)	Atlantic salmon (*S. salar*)	RRSQARKCSRGNGGKIGSIRCRGGGTRLG (29)	+	+	[2]
rtCath-1(Cathelicidin)	Rainbow trout (*Oncorhynchus mykiss*)	RRSKVRICSRGKNCVSRPGVGSIIGRPGGGSLIGRP (36)	+	+	[2]
rtCath-2(Cathelicidin)	Rainbow trout (*O. mykiss*)	RRGKDSGGPKMGRKNSKGGWRGRPGSGSRPGFGSGI (36)	+	+	[2]
LEAP-2	Channel catfish (*Ictalurus punctatus*)	MTPLWRIMGTKPHGAYCQNNYECSTGICRKGHCSFSQPIIS (41)		+	[45]
LEAP2	Atlantic salmon (*Salmo salar*)	MTPLWFTMGTKPYGAYCLHNYECSTGICRGHCMFSQPIKS (40)		+	[46]
LEAP2	Grass carp (*Ctenopharyngodon idella*)	MTPLWFIMGTKPHGAYCQNHYECSTGICRKGHCSYSQPINS (41)		+	[46]
LEAP2	Medaka (*Oryzias latipes*)	MTPLWFIMSSKPSGAFCQNNFECSTGFCRAGHCATNQRSEAVKY (44)		+	[46]
LEAP2	Winter flounder (*P. americanus*)	MTPLWFIMSSKPFGAYCQNNYECSTGLCRAGYCSTSHRASEPVNY (45)		+	[46]

	LEAP-2A	Carp (*Cyprinus carpio*)	MTPLWFIMGTKPHGAYC QNNYECSTGICRKGHCSY SQQPIHS (42)		+	[46]
	LEAP-2A	Rainbow trout (*Oncorhynchus mykiss*)	MTPLWRTMGTKPYGAYC LNNYECSTGICRGGHCMF SQPIKS (41)		+	[47]
	LEAP-2A	Zebra fish (*Danio rerio*)	MTPLWFTVGTKPHGAYC QNNYECSTGICRMGHCSY QPVNS (40)		+	[46]
	LEAP-2B	Carp (*C. carpio*)	MSPLWFIMGFKPYGAYC HDNIECITGLCRNGGHCSF NEPVHS (42)		+	[46]
	LEAP-2B	Rainbow trout (*Oncorhynchus mykiss*)	MTPLWRTMGTKPYGAYC RDHFECSTQICRRGHCAL SGAVHS (41)		+	[47]
	LEAP-2B	Zebra fish (*Danio rerio*)	MSPLWFTMGYKPYGAHC HDNIECNTCFCRNCQCSF NEAVHS (41)		+	[46]
histone-like	H2B	Atlantic cod (*Gadus morhua*)	Sequence not available (13 kDa)	+	+	[24]
	H2B	Rainbow trout (*Oncorhynchus mykiss*)	VSEGTHAVTKYTSSK (15)			[48]
	Hipposin	Atlantic halibut (*Hippoglossus hippoglossus*)	SGRGKTGGKARAKAKTR SSRAGLQFPVGRVHRLLR KGNYAHRVGAGAPVYL (51)	+	+	[49]

HLP1	Rainbow trout (*Oncorhynchus mykiss*)	PDPAKTAPKKGSKKACG (17)				[48]
Myxinidin, H3	Hagfish (*Myxine glutinous*)	GIHD/HILKYGKPS	+	+	−	[20]
Oncorhyncin II	Rainbow trout (*Oncorhynchus mykiss*)	KAVAAKKSPKKAKKPATPKKAAKSPKKVKKPAAAAKKAAKSPKKATKAAKPKAAKPKAAKAKKAAPKKK (69)	+	+	−	[50]
Parasin-1	Catfish (*Parasilurus asotus*)	KGRGKQGGKVRAKAKTRSS (19),	+	+	+	[51-52]
SAMPH1	Atlantic salmon (*Salmo salar*)	AEVAPAPAAAAPAKAPKKKAAAKPKKAGPS (30)	+	+		[53]

3. Gene engineering

Currently, a scalable method of active production is required in order to commercialize the fish-derived peptides. And the expense of peptide synthesis limits this form of production to small quantity applications, such as laboratory experimentation. A solution to this problem is to utilize the recombinant methods to heterologously express the antibacterial peptides in bacteria in inactive form. Recombinant AMP expression is highly valuable for structural studies. In addition, more recently researches on constructing aquatic animal immunospecific cDNA libraries and expressed sequence tag (EST) are increasing [54-56].

3.1 Escherichia coli expression system

Many host cells have been selected for expression of AMPs, but Escherichia coli has been become as one of the most popular. recombinant bioreactors due to its fast growth rate and well established expression systems. It is capable of express diverse proteins at high level, and the target protein is also easy purified. Due to transcriptional problem or toxicity of the expressed peptides, at present, there is a paucity of information concerning direct expression of small peptides in *Escherichia coli* [57-58]. The invention of fusion protein technology, which fuses the targeted peptide to a variety of tags or charged pro-sequences at the N-terminus of AMPs, solves these problems successfully. Fusion protein expressed by host cell can reduce original toxic and improve host expression level [59-60].

Srinivasulu had cloned several plasmid constructs encoding cysteine-rich peptide hepcidin from Japanese flounder, *Paralichthys olivaceus*, in inclusion bodies or the periplasmic space of *Escherichia coli* [61]. The results of their testing expression show that tobacco etch virus (TEV) protease cleavage can remove an N-terminal hexahistidine tag

and the recombinant His-hepcidin fusion peptide monomer showed better antimicrobial activity. Piscidins, Isolated from mast cells of hybrid striped bass, was recombinant expressed in *Escherichia coli*. Fusion partner of the recombinant production was cleaved by yeast ubiquitin hydrolase and the yield of the peptide was about 1.5 mg per liter of minimal medium [34].

3.2 Yeast expression system

Yeast is a typical eukaryotic expression system. Compared with *Escherichia coli*, yeast has the follow advantages: its regulatory mechanism of gene expression is more comprehensive, produces no endotoxic, embraces dual characteristic of prokaryotic and eukaryotic expression systems, and so on. Several aquatic animal AMPs have been successfully expressed in yeast, including penaeid shrimp, *Portunus trituberculatus, Mytiloida* [62-64]. Yin transformed the mature peptide of orange-spotted grouper epinecidin-1 and expressed the recombinant in *Pichia pastoris* SMD1168 successfully [65]. Then black sea bream hecipin, also expressed successfully in *Pichia pastoris* [66]. However, yeast is not perfect in fish AMPs recombinant expression. During the recombinant expression of winter flounder pleuricidin and hepcidin, target transcription was detected, but they have no expression product or antibacterial activity [67].

4. Mechanisms of AMPs action

With good thermal stability and hyperresistibility of acid, alkali and ionic strength, AMPs have been studied comprehensively and thoroughly. It is indisputable that the research on mechanisms of AMPs will be a scientific hot issue. Antimicrobial activity of AMPs is selective. Different membrane compositions and structures between prokaryotic and eukaryotic cells lead to AMPs' selective toxicity [68], however, precise mechanisms of

antimicrobial activity for many AMPs still need to be confirmed.

4.1 Membrane permeation

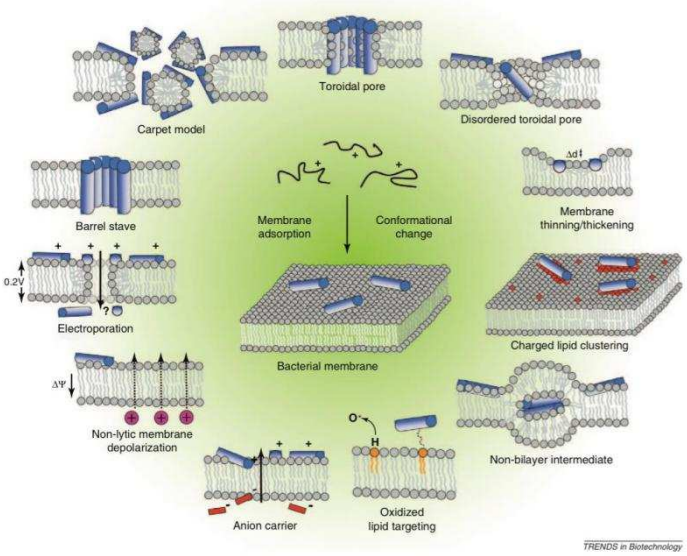

Figure 1. Mode of action for membrane permeation antimicrobial peptide activity [69].

Commonly, most AMPs share some similar physical features (such as a cationic charge and a significant proportion of hydrophobic residues), which make it easy to combine with bacterial cell membranes by electrostatic interactions and receptor mediating mechanism [70]. There are many models of peptide-membrane disruption (Figure 1), and the most important antimicrobial mechanisms include barrel-stave model, carpet model and toroidal pore model.

The first is barrel-stave model [69, 71]. Peptides bind with target membrane and make molecular recognition. When surface density of bound peptide reaches a critical threshold, the recognized membrane-bound monomers insert themselves perpendicularly across lipid bilayer to form peptide-lined pores and the following additional peptides increase the pore size. AMPs of this model usually have α-helixes or β-sheets lamellar in secondary structures [72]. The barrel-stave model mechanism involves four major procedures: (1) binding of the monomers to the cell membrane in a helical structure, (2)

molecular recognition between membrane-bound monomers that leads to their assembly at low density of bound peptide, (3) insertion of at least two assembled monomers into the membrane to initiate the formation of a pore, and (4) progressive recruitment of additional monomers to increase the pore size [71]..

The second is carpet model [71, 73-74]. In this model, peptides bind onto the surface of the target membrane and cover it or part of it in a carpet-like form. In contrast to the barrel-stave mechanism, the peptide does not insert into the hydrophobic core of the membrane, but rather binds to the phospholipid headgroups. Driven by electrostatic interaction, positively charged peptides interact with negatively charged phospholipid head groups. Then rotation of the molecule leads to reorientation of the hydrophobic residues to form a pore. Additional peptides come across the membrane. Finally, disintegrating the membrane by disrupting the bilayer curvature leads to micellization.. A prerequisite condition for carpet model mechanism is that a threshold concentration has been reached. Carpet model is the most common AMPs acting mechanism of killing Gram-negative bacteria and parasite.

The third is toroidal pore model [74-76]. In toroidal pore model peptides also insert perpendicularly in lipid bilayer, but the difference from the barrel-stave model is that it is always associated with the lipid head groups. This induces the lipid monolayers to bend continuously from the top to the bottom to form peptide-and-lipid-lined pores, as a result the peptides are embedded among the lipid head groups and the water core is lined by both the inserted peptides and the lipid head groups. Recent studies also demonstrated the mutual influence of lipid and peptide with regard to pore formation, while the peptide promotes the acquisition of curvature, the lipid organization modulates peptide

conformation.

Numerous structure-function studies have indicated that α-helix AMPs generally present uninterrupted hydrophobic surface, a key factor to cytotoxicity [77-78]. The sufficient lengths of α-helices make it easy to span the membrane bilayers. This leads to hydrophobic portion of the helices and the lipid acyl core mismatch with each other [79-80]. So membrane permeation is indispensable to the mechanisms of α-helix AMPs. But an AMP always works through mix-mechanisms. Tachyplesin, derived from horseshoe crabs, is a typical example. Brogden found that tachyplesin not only works with membrane, but also interferes with DNA–protein interactions through binding the minor groove of DNA[81].

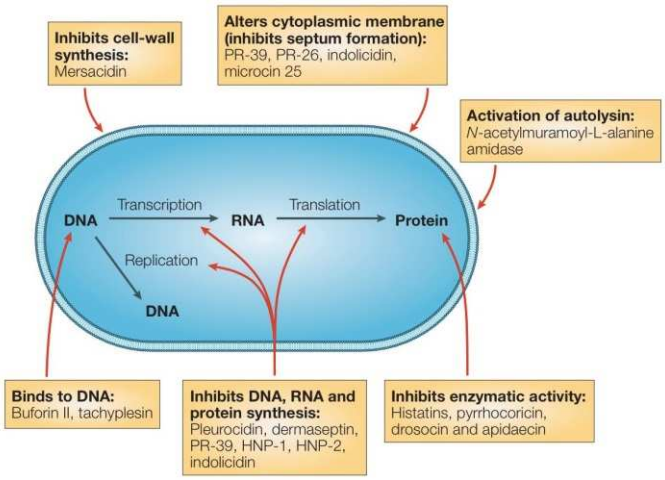

Figure 2.Mode of intracellular antimicrobial peptide action. *Escherichia coli* is shown as an example in this figure [76]

4.2 Intracellular action

Although antibacterial mechanism of the most AMPs is working through membrane permeation interaction, but a few of AMPs can kill bacteria without destroying the cell

membranes [82].This illustrates membrane permeation interaction is not the only way of antibacterial mechanism. At present, a lot of research results have showed that AMPs can bind with intracellular targets, disrupt the normal metabolism of cells and finally kill the bacteria Intracellular interactions involve lots of paths (Figure 2), such as binding with nucleic acid, inhibiting DNA replication, RNA synthesis and enzymatic activity; altering cell-wall and cytoplasm membrane formation to inhibit cell division, activating of autolysis, etc. In addition, Trinetta et al has proved that Sakacin A purified from *Lactobacillus sakei* could act on different intramolecular bonds of peptidoglycan by mass spectrometry analysis [83].

5. Application

The direct antimicrobial functions of several fish AMPs were reported. Almost all AMPs show direct antibacterial or bacteriostatic functions against several gram-negative and -positive strains. In addition, a few reports showed the antiviral functions of AMPs[84]. Nowadays, diverse fish-derived AMPs have been found continuously. It not only plays important roles in agriculture and pharmaceutical industry, but also has potential applications in the field of aquatic products due to its specific antibacterial mechanism and low resistance occurrence rate. However, most researches on inhibitory effects of fish-derived AMPs focus on pathogens in medical treatment and breeding. For example, fish hepcidins are active against a wide variety of bacteria at the low μM range, including potent activity against a large number of fish pathogens. This includes rapid killing kinetics against *Pseudomonas stutzeri* and *S. aureus* [1]. The histone-derived H2B peptide from Atlantic cod was reported to have antimicrobial functions against the fish pathogens, *Aeromonas hydrophilia* and *Saprolegnia* spp [24]. Derived from hybrid striped

bass, motonecidin is effective against 45 microorganisms, containing *Listeria monocytogenes*, *E. faecalis* (vancomycin-resistant enterococcus), *S. aureus* (methicillin-resistant *S. aureus*). The MIC of motonecidin is 1.25-2.5 μM [15]. Grammistins can inhibit growth of *V. parahemolyticus*, the MIC is 12.5-50 μM [85]. Yet, investigation on foodborne pathogens is still insufficient at present. In other ways, the antiviral functions of the β-defensin (BD)-1 peptide was demonstrated against viral hemorrhagic septicemia virus (VHSV) infection in rainbow trout [23], and TH1-5 from tilapia and epinecidin-1 from grouper showed antiviral functions against fish nervous necrosis virus (NNV) infection. The possibility of using fish-derived AMPs as model molecules to develop aquaculture antiviral agents was recently reviewed [86]. The genomic sequences of fish-derived AMPs can serve as a model to investigate the evolution of genes in different organisms. A recent report attempted to research the evolutionary process of fish hepcidin [87]. In addition, Some research has reported that AMPs can serve as a source for non-contaminated coatings of food packages. The use of chrysophsin-1 and -3 as self-decontaminating agents in an acrylic coating system killed both gram-negative and -positive bacteria, revealing that they have diverse applications [88]. It is expected that a better and deeper understanding of the antimicrobial mechanism of fish-derived AMPs will definitively result in safer food in the near future. Following a knowledge-based approach, new biopreservation strategies as well as unique biotechnological applications of these natural antimicrobials are envisaged.

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