Minireview

Postbiotics Applications as Infectious Disease Control Agent in Aquaculture

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Received 2 July, 2019/Accepted 19 August, 2019

Aquaculture is developing so fast that infectious disease outbreak happens regularly. Antibiotic treatment results in development of antibiotic resistance pathogens, thus cause urgent action in searching of other alternative treatment method. Postbiotic was one of the explored strategies among various proposed alternatives. Due to its benefits in agriculture industry, it may be useful in aquaculture industry. Although many reviews were reported on other alternative strategies, the review on postbiotic in aquaculture is limited. This mini review provides an overview of different postbiotics as aquaculture disease control agents. Peptides and exopolysaccharides have antimicrobial properties against bacterial pathogens. Then, short chain fatty acids have both antimicrobial activities against bacterial pathogens and immunostimulating effects to aquatic organism. Vitamins, peptidoglycan and lipopolysaccharide are reported as immunostimulants. Finally, cell surface proteins and teichoic acid can act as vaccine.

Key words : Postbiotic / Aquaculture / Disease Control / Alternative Treatment Method.

INTRODUCTION

Aquaculture is an important industry. Global aquaculture production in 2016 was 110.2 million tonnes (USD 243.5 billion), occupying 46.8% of the combined production of fisheries and aquaculture, with growth rate faster than many food production sectors (FAO, 2018). However, continuous development of aquaculture causes rampant infectious disease outbreak, may be due to movements of hatchery produced stocks, introduction of new cultured species and trade liberalization (Subasinghe, 2009). To control disease outbreak, chemotherapeutants treatment and control strategies such as vaccination were employed. However, use of chemotherapeutant such as antibiotic results in development of antibiotics resistance microbial pathogens, and vaccination was mainly as prophylactic and limited for immunocompromised organisms (Subasinghe, 2009).

Therefore, alternative disease control agent such as postbiotic was explored.

Postbiotics are soluble factors secreted by living bacteria or released after bacterial lysis (Aguilar-Toalá et al., 2018). Currently, application of postbiotic in pharmaceutical products, commercial food-based products and terrestrial agriculture have been reviewed (Aguilar-Toalá et al., 2018). However, review of application of postbiotic in aquaculture is limited, even though there is vast literature addressing the use of short chain fatty acids and organic acids, peptides, teichoic acids, peptidoglycan, exopolysaccharides, cell surface proteins and vitamins in aquaculture. Hence, this mini review provides new information regarding antimicrobial and health promoting properties of postbiotics, either *in vitro* or *in vivo* from different bacterial species, in aquaculture animals.

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SHORT CHAIN FATTY ACIDS

Short chain fatty acids (SCFAs) are organic acids containing aldehyde and one or more carboxyl groups. SCFAs such as propionic acid and butyric acid are commonly used as salts in aquaculture. Propionic acid could be produced by *Propionibacterium* and butyric acid is produced by *Clostridium tyrobutyricum*. Propionate and butyrate salts supplementation in white leg shrimp (da Silva et al., 2013; da Silva et al., 2016) and butyrate salts in gilthead sea bream (*Sparus aurata*) (Piazzon et al., 2017) and grass carp (*Ctenopharyngodon idella*) (Tian et al., 2017) showed modulation in gut microbiota. SCFAs salts protected hosts from infectious diseases. Butyrate salts induced protection in grass carp, white leg shrimp (*Litopenaeus vannamei*) and gilthead sea bream from enteritis morbidity caused by *Aeromonas hydrophila*, *Vibrio alginolyticus* and *Photobacterium damsela* ssp. *piscicida* respectively (Tian et al. 2017; Ramírez et al. 2017; Piazzon et al. 2017). Protection from pathogens primarily due to stimulation of immune responses. Stimulation of immune responses was shown in Caspian Sea white fish (*Rutilus frisii kutum*) (Hoseinifar et al., 2016), zebra fish (*Danio rerio*) (Safari et al., 2016) and white leg shrimp (Pourmozaffar et al., 2017; da Silva et al., 2016) through propionate or propionic acid supplementation. In other reports, common carp (*Cyprinus carpio*) (Liu et al., 2014), European sea bass (*Dicentrarchus labrax*) (Rimoldi et al., 2016), grass carp (Tian et al., 2017), Nile tilapia (*Oreochromis niloticus*) (Ali et al., 2018) and white leg shrimp (da Silva et al., 2016) showed stimulation in their immune responses through butyrate supplementation.

PEPTIDES

One of the common peptides from bacteria is bacteriocin, which is an antimicrobial protein. The studies for bacteriocin are very extensive, due to its potential to replace antibiotics as an alternative aquatic diseases treatment. Bacteriocins against aquatic pathogens are shown in Table 1. Bacteriocins have good potential to replace antibiotics. Bacteriocins are mostly active against closely related bacteria species, leaving non-related or beneficial bacteria (Deraz et al., 2005). Therefore, reducing problem such as the development of antibiotic resistant bacteria. In addition, bacteriocins as proteinaceous agents can be digested by proteolytic enzymes such as trypsin, ficin, pepsin, papain, and proteinase K in digestive tract (Deraz et al., 2005). Therefore, problem such as antibiotic residue in aquaculture food will not cause allergic reactions and other medical problems when consumed.

EXOPOLYSACCHARIDES

Exopolysaccharides (EPS) is polymer secreted into external environment. EPS of *Bacillus cereus* and *Brachy bacterium* sp. isolated from Asian seabass (*Lates calcarifer*) showed antimicrobial properties (Orsod et al., 2012). However, EPS of *B. licheniformis* strain of marine sponge (Sayem et al., 2011) and *Pseudomonas stutzeri* (Wu et al., 2016) showed antibiofilm properties, with EPS from *P. stutzeri* reduced virulence factor of *P. aeruginosa*. Therefore, EPS could decrease the risk of pathogenic infection to aquaculture animals.

VITAMINS

Vitamin C or ascorbic acid is a co-factor for biological processes such as collagen synthesis and cellular functions related to neuromodulation, hormone and immune systems (Mastan, 2015). Therefore, vitamin C is widely used as immunostimulant in aquaculture. Vitamin C was industrially produced by *Ketogulonicigenium vulgare* and *Bacillus* spp. It was reported to improve immune responses (non-specific and specific immunity) and increased infectious disease resistance in rainbow trout (*Oncorhynchus mykiss*) (Wahli et al., 1998), rohu (*Labeo rohita*) (Tewary and Patra, 2008), gilthead sea bream (Mulero et al., 1998), mrigal (*Cirrhinus mrigala*) (Sobhana et al., 2002) and channel catfish (*Ictalurus punctatus*) (Li and Lovell, 1985).

PEPTIDOGLYCAN

Peptidoglycan (PG) is a polymer of sugars and amino acids, and is reported as immunostimulant in aquaculture. PG from *Bifidobacterium* sp., *Brevibacterium lactofermentum* and *B. thermophilum* had been tested in sea cucumber (*Apostichopus japonicus*) (Zhang et al., 2014), Japanese flounder (*Paralichthys olivaceus*) (Jorge et al., 2006) and rainbow trout (Matsuo et al., 1993). Generally, PG showed enhanced immune responses and protection against pathogens. Modification of PG from *B. thermophilum* through hydrolysis showed similar effects in white leg shrimp (Song et al., 2013).

LIPOPOLYSACCHARIDES

Lipopolysaccharides (LPS) or endotoxin is a molecule of lipid and polysaccharide, and also reported to be used as immunostimulant in aquaculture. LPS from *Escherichia coli*, *V. anguillarum*, *Edwardsiella tarda*, *A. hydrophila* and *V. harveyi* have been tested in striped catfish (*Pangasianodon hypophthalmus*) (Bich Hang et

TABLE 1. Bacteriocins against aquatic pathogens.

Bacteriocin	Producer Strain	Inhibited Strain	References
BLIS	<i>Roseobacter</i> sp. BS107	<i>Vibrio</i>	Ruiz-Ponte et al. (1999)
Carnocin U149	<i>Carnobacterium</i> sp.	<i>Lactobacillus</i> , <i>Lactococcus</i> , <i>Pediococcus</i> , <i>Carnobacterium</i>	Stoffels et al. (1992)
Divergin M35	<i>Carnobacterium divergens</i> M35	<i>Carnobacterium</i> , <i>Listeria</i>	Tahiri et al. (2004)
Piscicocin V1a, Piscicocin V1b	<i>Carnobacterium pisciocola</i> V1	<i>Lactobacillus</i> , <i>Listeria</i> , <i>Enterococcus</i> , <i>Pediococcus</i> , <i>Carnobacterium</i>	Bhugaboo-Vial et al. (1996)
BLIS	<i>Vibrio</i> sp. NM 10	<i>Photobacterium</i>	Sugita et al. (1997)
BLIS	<i>Vibrio mediterranei</i> 1	<i>Vibrio</i> , <i>Aeromonas</i>	Carraturo et al. (2006)
BLIS	<i>Vibrio harveyi</i> VIB 571	<i>Vibrio</i>	Prasad et al. (2005)
Harveycin	<i>Vibrio harveyi</i> (formerly known as <i>Beneckea harveyi</i> SY)	<i>Vibrio</i>	McCall and Sizemore (1979)
IW1	<i>Vibrio vulnificus</i>	<i>Vibrio</i>	Shehane and Sizemore (2002)
BC1		<i>Vibrio</i>	Kumar and Arul (2009)
BC2		<i>Vibrio</i> , <i>Plesiomonas</i> , <i>Escherichia</i>	Ruiz-Ponte et al. (1999)
Phocaeicin PI80	<i>Streptococcus phocae</i> P180	<i>Escherichia</i> , <i>Listeria</i> , <i>Vibrio</i>	Stoffels et al. (1992)
-	<i>E. coli</i>	<i>Aeromonas</i> , <i>Citrobacter</i> , <i>Edwardsiella</i> , <i>Flavobacterium</i> , <i>Pseudomonas</i> , <i>Vibrio</i>	Lee et al. (2014)
-	<i>Enterobacter cloacae</i> , <i>Cronobacter sakazakii</i>	<i>Vibrio</i>	Thu Thuy et al. (2014)
-	<i>Bacillus subtilis</i> KY808492	<i>Salmonella</i> , <i>Vibrio</i>	Ashwitha et al. (2017)
Enterocin MC13	<i>Enterococcus faecium</i> MC13	<i>Listeria</i> , <i>Vibrio</i>	Satish Kumar et al. (2011)
Bacteriocin JFP2	<i>Bacillus amyloliquefaciens</i> JFP2	<i>Aeromonas</i>	Kim et al. (2017)
-	<i>Lactobacillus lactis</i> ssp. <i>lactis</i>	<i>Listeria</i> , <i>Brochothrix</i> , <i>Salmonella</i> , <i>Staphylococcus</i> , <i>Bacillus</i> , <i>Aeromonas</i> , <i>Pseudomonas</i> , <i>Escherichia</i>	Sahnouni et al. (2014)
TW34 bacteriocin	<i>Lactococcus lactis</i> TW34	<i>Lactococcus</i>	Sequeiros et al. (2015)
-	<i>Bacillus subtilis</i> NCIMB 3610	<i>Enterococcus</i> , <i>Vibrio</i> , <i>Photobacterium</i>	Touraki et al. (2012)
Garvivin A	<i>Lactococcus garvieae</i> 21881	<i>Lactococcus</i>	Maldonado-Barragán et al. (2013)

al., 2013), Atlantic salmon (*Salmo salar*) (Dalmo and Seljelid, 1995), Asian stinging catfish (*Heteropneustes fossilis*) (Pattnaik et al., 2001), rainbow trout (Nya and Austin, 2010), common carp (Selvaraj et al., 2004), tiger shrimp (*Penaeus monodon*) (Genio et al., 2014; Traifalgar et al., 2010; Sritunyalucksana et al., 1999) and Chinese white shrimp (*Fenneropenaeus chinensis*) (Qiao et al., 2013) showed stimulation at their immune responses (upregulation of immune related genes, non-specific immunity, specific immunoglobulins) and increased the survival from pathogens infection.

CELL SURFACE PROTEINS

Cell surface proteins such as outer membrane protein (OMP) is commonly used as vaccine in aquaculture. OMP (*A. hydrophila*, *V. harveyi*, *Stenotrophomonas maltophilia* & *V. alginolyticus*) were tested in aquaculture animals such as rohu (Yadav et al., 2018), channel catfish (Abdelhamed et al., 2017; Wang et al., 2016), goldfish (*Carassius auratus*) (Divya et al., 2015), turbot (*Scophthalmus maximus*) (Wang et al., 2011) and tiger shrimp (Maftuch et al., 2013) showed stimulation towards immune responses (up-regulation of immune-related genes, non-specific parameters and specific antibodies), reduced bacterial load and mortality. Recombinant OMPs (*Flavobacterium columnare*, *V. anguillarum*, *Piscirickettsia salmonis* & *A. hydrophila*) were successfully synthesized and tested in grass carp (Luo et al., 2016), rohu (Hamod et al., 2012), coho salmon (*Oncorhynchus kisutch*) (Kuzyk et al., 2001) and common carp (Maiti et al., 2012). Development of polyvalent vaccine with OMPs from *A. hydrophila* (Ni et al., 2010), *V. parahaemolyticus* (Li et al., 2010) and *V. alginolyticus* (Nehlah et al., 2016) has been successful.

TEICHOIC ACIDS

Teichoic acid is bacterial copolymer between glycerol phosphate or ribitol phosphate with carbohydrates. It has potential to be vaccine because antibodies against lipoteichoic acid (LTA) of *Enterococcus faecalis*, an aquatic pathogen, showed opsonization against other Gram-positive species, suggesting function to immunize against multiple Gram-positive pathogens (Rahman et al., 2017; Theilacker et al., 2012). However, immunological studies by Theilacker et al. (2012) was not done in aquatic animal, and are subjected to further study.

CONCLUSION

Infectious disease is a serious issue in aquaculture development. Postbiotics such as SCFAs, peptides, exopolysaccharides, vitamins, peptidoglycan,

lipopolysaccharides, cell surface proteins and teichoic acids are potential alternative disease control agents in aquaculture.

ACKNOWLEDGEMENT

The study was supported by the Ministry of Education Malaysia under the Fundamental Research Grant Scheme (FRGS) No.: FRG0454-STWN-1/2016 and FRG0502-1/2019. This study was also received support from the JSPS Core-to-Core Program "Building up an international research network for successful seed production technology development and dissemination leading South-East Asian region".

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