Using Probiotics as an Eco-Friendly Strategy for Controlling Diseases in Aquaculture

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Abstract – *Aquaculture industry is one of the rapidly growing industries providing ample revenue for producers and wholesome nutrition to consumers. Indiscriminate use of antibiotics to control diseases in aquaculture has led to serious ecological concerns. Pathogenic microorganisms are increasingly becoming resistant towards these antibiotics. Probiotics are either live or dead or even a component of a microorganism that is capable of conferring benefits to their host. Probiotic organisms are naturally found in animals and are known to elicit beneficial behavior such as fighting off pathogens, aiding in the digestion of food consumed by host, immunomodulation, producing beneficial compounds, etc. Ever since use of probiotics started gaining attention for their benefits to human health, they have been explored for their use in animals as well. Multitude of research conducted on use of probiotic microorganisms on different animals has brought them to the position of eco-friendly alternative for antibiotics and also as health promoting agents. Use of probiotics as dietary supplements to improve survival rates of fishes has gained much attention during the past decades. Probiotics, prebiotics and synbiotics were showed as the most promising feed supplements for control or treatments of bacterial, viral and parasitic diseases. This review takes a comprehensive approach on various aspects of aquaculture such as diseases in aquaculture, detailed view of potential probiotic microorganisms that can fight off diseases and their mechanism of their action. Furthermore, this paper affirms the importance of use of probiotics in a fast-growing industry like aquaculture in developing sustainable strategies for overall development of the industry.*

***Key Words*: Antibiotic resistance, aquaculture, fish and shellfish diseases, probiotics, immune response, disease control, probiotics in aquaculture**

1. INTRODUCTION

Probiotics are living cultures of microorganisms such as bacteria or yeast, which are known to fight against several pathogens and promote general immunity and digestion by colonizing in the gut on consumption. The term "probiotics" came from the two Greek words "pro" and "bios" meaning "for life". Parker (1974) was the first to define probiotics as organisms and substances that affect microbes harboring intestine. [1] Their presence and activity in the intestine is known to impact the overall health of the individual as they, in symbiosis with the host, are involved in metabolism of nutrients, drug and xenobiotics. Apart from that, they are also known to act as protective barriers against pathogens and act as immunomodulators. [2] In humans, they have shown promising results against onset or relapse of gastrointestinal tract associated diseases and respiratory tract infections and have also been used for treating medical conditions. [3] [4] Probiotics as feed additives has shown to be very effective against several bacterial pathogens in livestock as well as in aquaculture. [5] [6] The FAO/WHO definition of a probiotic— "live microorganisms which when administered in adequate amounts confer a health benefit on the host" [7]. Several microorganisms are known to act as probiotics which can be narrowed down to seven core genera of microbes i.e., *Streptococcus, Bacillus, Escherichia, Enterococcus, Saccharomyces, Bifidobacterium, Lactobacillus.* Commercially available_probiotics consist of about 1 to 10 billion CFU per dose [8]. Probiotics are consumed regularly to replenish the micro flora which is lost from day-to-day activities of the body and establish a healthy gut.

Aquaculture, also known as aquafarming is a multidisciplinary subject dealing with the process of rearing, breeding and harvesting aquatic animals and plants of commercial and recreational value on land with arrangements that suit the type of organism being reared [9]. Certain important examples include catfish, salmon, lobster, crabs, mollusks, seaweeds, carps, etc. Packed with high amounts of proteins, vitamins and minerals, the consumption of seafood has been linked to numerous health benefits. Fishes are great source of omega-3 fatty acids and low in 'bad' fats which makes it a highly nutritious and an incredibly important food [10]. Pescatarianism grew as a popular diet choice among people who looked to avoid intake of animal meat containing saturated fats by incorporating seafood as the only source of meat in an otherwise vegetarian diet, thereby not compromising their protein intake Aquaculture has a very broad scale ranging from creating a simple backyard pond that supports growth of fishes to making integrated systems of tanks and pipes that supports growth of multiple organisms. [11]. The former can be used to meet a family's needs while the latter can be used for large scale marketing and profits. Aquaculture is now a Billion-dollar company with China standing as the largest producer in the world (63.70 MMT) and India standing at fourth (5.70 MMT).

As the population escalated with each passing year, so did the demand for seafood. In India alone the Fish and Seafood supply per person per year increased from 1.86 Kg in 1961 to 6.90 Kg in 2017.

1. Methods of Aquaculture

I. The culturing can be done in symbiosis with plant culture called aquaponics. Aquaponics is a process where aquaculture of organisms like fishes goes simultaneously with the growing of plants in water (hydroponics). The main significance of this type of combination culture lies in the way the water is being circulated in the entire system [12]. The water containing nitrogenous wastes produced by the fishes is flushed out of their tanks through a pump that takes the same water to the place where plants ae being grown so that the denitrifying bacteria can act on it and break down toxic nitrogenous wastes into nitrated and nitrites. This water which now is devoid of wastes is recirculated back to fish tanks. Hence there is constant movement of water back and forth from the aquaculture system to hydroponic system [13].

II. Another effective type of aquaculture used widely by the growers is the integrated multi-trophic aquaculture (IMTA) where animals of different trophic levels in the proximity of each other [14]. This method is in a way similar to aquaponics. The difference lies in the fact that since different organisms are present in the same system, it enables them to feed on uneaten food, breakdown wastes, recirculate the nutrients and extract the by-products to make fertilizer. Unlike aquaponics, farmers here combine the culturing of fed species (most finfish species) with non-fed ones (carps, filter-feeders, seaweeds). IMTA can be practiced either on land, offshore or inshore. Offshore IMTA has been seen as an environmentally friendly form of aquaculture [15].

2. *Diseases in Aquaculture*

Since the fishes are kept in unnatural habitat with cramped conditions, they are vulnerable to the outbreak of infectious diseases which can wipe out major populations. The diseases in fish fall under two categories: The disease caused by native pathogens of the local environment and the ones caused by non-native or exotic pathogens normally not found in that area. [16] The preventive and control measures of such diseases include maintenance of hygiene and treatment with antibiotics. But, unlike animals and humans, the availability of drugs to treat fishes is only a handful. In the United States, only two drugs have been approved for their treatment due to environmental concerns. [17]

Table -1: Diseases in Aquaculture

DISEASE	PATHOGEN	HOST	SIGNS
Vibriosis	*Vibrio vulnificus. Aliivibrio salmonicida. Photobacterium damselae.*	Eel, Anguilla, Salmon, Tuna, shrimp species, etc.	Erosion and darkened skin and fins, hemorrhage to intestines, spleen and muscle.
AEROMONIASIS	*Aeromonas salmonicida, A.caviae, A.hydrophila, A.sobria, A.veronii, A. jandaei*	Salmonids, Tilapia, Catfish, Puntius, Rohu, etc.	Skin ulcers, fin discoloration, swimming abnormalities, hemorrhagic septicemia.
EDWARDSIELLOSIS	*E. piscicida, E. tarda, E. anguillarum E. ictaluri*	Pangasius hypophthalmus, Tilapia, Eel, salmon, trout, Catfish	Interstitial nephritis, suppurative hepatitis, purulent inflammation in the spleen, abscesses filled necrotic substances and gas (in catfish).
ENTERIC RED MOUTH (ERM)	*Yersinia ruckeri*	rainbow trout and other salmonids	Subcutaneous hemorrhaging of the mouth, eyes and fins leading to reddening of mouth, gill tips, and fins, eventually eroding the

			jaw and palate.
PSEUDOMONIASIS	*Pseudomonas anguilliseptica, Pseudomonas fluorescens*	Eel, Tilapia, Cod, Trout, Trench, Silver carp, Bighead carp.	hemorrhages exophthalmia, Ulcers, hemorrhagic septecemia ascites.
MYCOBACTERIOSIS	*Mycobacterium marinum, Mycobacterium fortuitum*	Striped bass, tilapia, cyprinids, catfish, snakehead,	Wasting exophthalmia, skin lesions, Lethargy.
STREPTOCOCCOSIS	*Lactococcus garvieae*	Grey mullet, Rainbow trout, marine species like Japanese yellowtail.	Unilateral or bilateral exophthalmia, lack of appetite, lethargy, abnormal swimming.
FLAVOBACTERIOSIS	*Flavobacterium branchiophilum, Flavobacterium columnare*	Tilapia, Crypnids and various other freshwater fish species.	Bacterial Gill Disease- Pale swollengills and flared opercula Columnaris disease- Skin ulcers, loss of epidermis, white/cloudy patches as seen on gills.

3. PROBIOTICS IN AQUACULTURE

Use of various antibiotics to control the spread of diseases gave rise to food safety issues, environmental hazards, development of drug resistance in the pathogens etc. This led to an extensive research on the alternative methods of efficiently combating diseases without compromising the food and environmental safety. Thus, the use of probiotics as an alternative to the use of antibiotics gained immense attention. Since the market is always high in demand for superior quality, safe and healthy foods and with use of probiotics it became possible to provide innate health and immunity to help them fight diseases.

Extensive reports revealed the positive effects of probiotics on the hosts gut resistance including immune response, stress tolerance as well as disease prevention [18]. There are several mechanisms by which the probiotics work in conferring several benefits to its host such as competitive exclusion, providing immunity, production of antimicrobial molecules, competing for nutrients, etc. [19]. Applications can be either single or multiple strains along with a prebiotic, or even in combination with immunostimulants such as synbiotics, in dead or live forms.

4. SOURCES OF PROBIOTICS

The microorganism being used as a probiotic may or may not be of a host origin. Host derived probiotics are the microbes that have been isolated from the same species as the host whereas non-host probiotics are the ones that have been isolated from external environment or from a different species. Research has shown that a probiotic when given in proper amounts and time is capable of giving a great number of benefits irrespective of the origin. However, a host originated probiotic has advantages such as salinity, pH environment familiarity, etc. [20]

5. TYPES OF PROBIOTICS

A diverse array of microorganisms such as Gram-negative, Gram-positive, fungi, etc are capable of acting as probiotics. A few of them are discussed below.

5.1 GRAM-NEGATIVE BACTERIA-

1. *Aeromonas*- Although *Aeromonas* is capable of causing aeromoniasis in fishes, research has shown that oral administration of formalin-inactivated *Aeromonas hydrophila* cells increased its capacity of the ornamental goldfish to fight *A. salmonicida* [21]. Cultures of *Aeromonas sobria*, was found to trigger innate immunity of rainbow trout when it was incorporated into their feed for 14 days with a dose concentration of 5 x 10(7) cells g(-1) of feed [22]. Oral administration of A. veronii BA-1 isolated from common carp showed improved resistance against *A. hydrophila* at 1 × 108 cell g−1 of feed [23].

2. *Enterobacter*- Enterobacter is a genus of common Gram-negative, rod-shaped, non-spore-forming, facultative anaerobes found in soil, water, intestinal tracts of humans and animals [24]. A research carried out to find the effects of inactivated *Enterococcus faecalis* cells when fed to rainbow trout at a dose of 5 g kg−1 was found to decrease the mortality caused by *A. salmonicida* infection [25]. A study also demonstrated the potential use of *Enterobacter amnigenus* and its species as a probiotic in managing infections caused by *Flavobacterium psychrophilum* responsible for causing various diseases in aquaculture [26]. A host derived probiotic *Enterococcus casseliflavus* was found to be effective in conferring resistance to rainbow trout against *Streptococcus iniae* infection through immunomodulation [27].

3. *Pseudomonas*- These occur in natural marine waters, soil and belong to the class Gammaproteobacteria and naturally occur in the gut flora of healthy fishes. A study conducted in India suggested that *Labeo rohita* fishes suggested that a dietary supplementation with *Pseudomonas aeruginosa* [10(7) cfu g(-1)] successfully improved disease resistance [28]. In vitro studies in rainbow trout showed that vibriosis-caused mortality was reduced by administration of *Pseudomonas fluorescens* [29]. *Pseudomonas aeruginosa* strains that can degrade N-hexanoyl-L-homoserine lactone (AHL) were able to inhibit the biofilm formation during *V. parahaemolyticus* infection in zebrafish [30].

4. *Roseobacter*- These are rod shaped Gram-negative bacteria and belong to the genus Rhodobacteraceae. They are found in diverse marine habitats [31]. When turbot larvae were fed with rotifers incorporated with R*oseobacter* strain 27-4 along with a pathogen *Vibrio anguillarum* the Vibrio infection were significantly reduced indicating *Roseobacter* as a potential probiont [32]. Another research suggested that when *Roseobacter* species were tested for their antibacterial activity against different *Vibrionaceae* strains using agar well diffusion, they were found to give clear zones indicating an antibacterial activity. The *Roseobacter* was isolated from turbot larval tank walls and were found to be antagonistic to the vibrio strains [33].

5. *Shewanella*- These are rod shaped facultative anaerobes occurring in extreme temperature habitats such as very low temperature and high pressure [34]. A study conducted to check benefits of *Shewanella putrefaciens* as a probiotic organism proved that using it as a feed additive increased the production of goblet cells in *Solea senegalensis* [35]. An experiment suggested that a dietary supplement consisting of a combination of *Shewanella xiamenensis* and *S. xiamenensis* were found to increase resistance in grass carp against *A. hydrophila* infection [36].

6. *Flavobacterium*- These are found naturally in soil, water bodies and in the gut of healthy fishes. *Flavobacterium sasangense* (BA-3) isolated from intestine of common carp enhanced immune parameters of the carp and their capacity to resist *A. hydrophila* infection when fed for 28 days at a dose of 1 × 108 cell g−1 [37].

7. *Zooshikella*- A dietary supplementation of *zooshikella* species as a probiotic to olive flounder strengthened its innate immunity and disease resistance against an experimental *Streptococcus iniae* infection [38].

5.2 GRAM-POSITIVE BACTERIA-

1. *Lactobacillus*- The use of Lactobacillus species as a probiotic has been widely studied with respect to aquaculture owing to its huge benefits [39]. A research with six Lactobacillus species considered safe for human use were tested for their potential in aquaculture wherein they found the best effects of *L. rhamnosus* (ATCC 53103) and *L. bulgaricus* based on bile resistance, mucus penetration, mucus adhesion, and suppression of the pathogen [40]. Using *L. rhamnosus* as a feed supplement at 108 CFU g−1 and 1010 CFU g−1 in nile tilapia showed enhanced TNF alpha and IL-1 gene expression, and increased resistance to *Edwardsiella* infection indicating its importance as a probiotic [41]. Furthermore, when *L. acidophilus* was fed to juvenile African catfish at 3 × 107 CFU g−1 showed resistance against *Aeromonas hydrophila* gr2 and *Staphylococcus xylosus,* and *Streptococcus agalactiae* (2 × 106 CFU ml−1 intraperitoneal injection) [42]. A study aimed to check the potential use of *L. pentosus* PL11 (10^8 cfu g^{-1}) potential as an alternative to antibiotic showed its efficacy in improving health and growth of Japanese eel (A. japonica) [43]. Similarly, another study showed the immunomodylatory effects of *Lactobacillus pentosus* PL11 on Head kidney leukocytes of Japenese eel when experimentally challenged with *Edwardsiella tarda* infection [44]. Another study using *L. sakei* BK19 (2.2 × 107 CFU g−1) showed an insignificant decrease in mortality of experimentally infected rock bream (*Oplegnathus fasciatus*) with *Edwardsiella tarda* [45].

2. *Leuconostoc*- Generally is a coccus and exist in long chains. Found in many processed, fermented foods, milk and dairy products [46] . When *Leuconostoc mesenteroides* was used as one of the probiotics in rainbow trout, the fish showed reduced severity of furunculosis indicating increased and better immune response [47]. Another study

conducted by the same group found that *Lc. mesenteroides* isolated from rainbow trout intestine inhibited the growth of various pathogens [48]. However, some researchers have also studied about negative effects of the bacterium wherein they isolated *L. mesenteroides* from the intestine of rainbow trout failed to show resistance against lactococcosis [49]

3. *Lactococcus*- These are homofermentors belonging to lactic acid bacteria and are naturally found in dairy products and plants [50]. A recent study using *L. plantarum* FGL0001 and *L. lactis* BFE920, or single *L. lactis* BFE920 for 30 days as a feed supplement in olive flounder increased their capacity to resist *S. iniae* infection [51]. Administering a supplement of *L. lactis* to a brown trout that was experimentally infected with *Aeromonas salmonicida,* showed resistance against the infection by increasing immune parameters [52]. Similarly, research in olive flounder suggested that when *L. lactis* (108 CFU g−1) were given as feed additives heightened their immune response against *S. iniae* [53].

4. *Enterococcus*- It is a lactic acid bacterium that occurs in pairs (diplococcus). It is found in soil, water, plants, inside gastrointestinal tract of animals including humans, and have been explored as potential contender as probiotic in fishes [54]. Research suggested that incorporation of *E. faecium* SF 68 in European eel diet lowered the contraction of edwardsiellosis in the fish exposed to the pathogen [55]. Another study showed that *E. casseliflavus* when used as a feed supplement in juvenile rainbow trouts improved their health and resistance against *S. iniae* infection [56].

5. *Bacillus sps*- This genus has also been extensively studied for its use as a beneficial probiotic in aquaculture. A study conducted in India suggested that a supplementation of *B. subtilis* at 1.5 × 107 CFU g−1 to *Labeo rohita* increased its resistance against A. hydrophila infection [57]. Similarly, another research showed that a dietary supplementation of *B. subtilis* and *B. licheniformis* (BioPlus2B) to trouts increased their resistance to *Y. ruckeri* [58]. Furthermore, when rainbow trout were supplemented with *Bacillus subtilis* AB1 isolated from fish intestine for 14 days at 10(7) cells per gram provided resistance against an experimental *Aeromonas* sp infection [59]. *Bacillus circulans* PB7 isolated from *Catla catla* were fed to *Catla* fingerlings at dose of 2 x 10(4) (feed C1), 2 x 10(5) (feed C2), and 2 x 10(6) (feed C3) showed increased survival against *A. hydrophila* infection, highest survival being at C2 [60]. Another study stated that feeding *B. licheniformis* to tilapia increased their resistance to *Streptococcus iniae*. Another study suffested that a dietary supplement of *B. subtilis* HAINUP40 improved disease resistance of Nile tilapia when fed at 108 cfu/g [61]. Similarly, another study in Nile tilapia, *Oreochromis niloticus* suggested that when a supplementation of a mix of *B. subtilis* and *B. licheniformis* at 0 g kg−1 (CT), 3 g kg−1(BS3), 5 g kg−1 (BS5), 7 g kg−1 (BS7), and 10 g kg−1 (BS10) for four weeks improved overall health and immunological parameters of the fish specially at 10 g kg−1(BS10) concentration [62]. A study carried out to check probiotic effects of *Bacillus licheniformis* and *B. pumilus* on *Labeo rohita* suggested that intraperitoneal administration of components such as cell wall proteins and whole cell proteins of the two species of bacteria increased resistance of the fish against *A. hydrophila* infection [63].

6. *Carnobacteria*- These are rod-shaped lactic acid bacteria and can grow anaerobically [64]. A study suggested that *Carnobacterium maltaromaticum* isolated from the midgut of Atlantic cod could out-compete a *V. anguillarum* a pathogen [65]. A potential probiotic *Carnobacterium* sp. strain K1 isolated from gut of Atlantic salmon produced inhibited fish pathogens such as *Vibrio anguillarum* and *Aeromonas salmonicida* in vitro [66]. Also, dietary administration of *C. inhibens* at 5 × 107 cells g−1 K1 for 14 days reduced A. salmonicida, Vibrio ordalii and Yersinia ruckeri related mortalities in Atlantic salmon and rainbow trout [67].

7. *Pediococcus*- This is also a lactic acid bacterium found in pairs or tetrads and are used in fermentation processes [68]. A study found that incorporation of *Pediococcus acidilactici* into the diet of rainbow trout fry caused them to develop resistance against vertebral column compression syndrome (VCCS) [69]. Also, dietary administration of *P. pentosaceus* 4012 in groupers (Epinephelus spp.) significantly decreased the mortality after *V. anguillarum* infection [70]. Furthermore, *Pediococcus pentosaceus* strain (SL001) isolated from soil samples promoted immune response of the fishes and also exhibited antimicrobial activity against experimental *A. hydrophila* infection [71].

8. *Vagococcus*- These are non-spore forming cocci which can be either motile or non-motile [72] A study showed that when *V. anguillarum* challenged sea bass were supplemented with *Vagococcus fluvialis* (109 cfu g−1) for 20 days showed higher survival rate (42.3%) as compared to control group [73]. Similarly, another research also showed that when *Vagococcus fluvialis* were fed to gilthead sea bream (*Sparus aurata*) and European sea bass (*Dicentrarchus labrax*) showed increased immunomodulatory effects [74].

5.3 YEAST

A trial conducted to check the efficacy of *Debaryomyces hansenii* strain CBS 8339 as potential immune enhancers of an experimentally *Aeromonas hydrophila* infected leopard grouper (*Mycteroperca rosacea*) suggested when the fish were fed with an yeast supplemented diet, their resistance towards the infection increased by enhancing the immunity [75]. A group of scientists also found that addition of Baker's yeast in the diet of Galilee tilapia *Sarotherodon galilaeus* improved its resistance against water-born Cu toxicity and also improve its growth performance [76]. Another study wherein Nile tilapia that experimentally challenged *Aeromonas hydrophila* was supplemented with baker's yeast in its diet for 12 weeks showed to improve immunity and disease resistance when fed at 1.0–5.0 g yeast/kg diet.

6. MECHANISM OF ACTION OF PROBIOTICS

As discussed above, probiotics have immense importance in the field of aquaculture in providing them resistance against pathogenic bacteria, parasites and viruses. They do so by improvising their hosts immunological parameters in many different ways. They not only modify their immune system but are also found to adhere to mucosal epithelium of the gut thereby providing resistance against pathogens [77]. They can also increase the feed digestibility of the fishes by enhancing their production of digestive enzymes like proteases, lipases, amylases [78].

Immunomodulation- The innate immune response which is also the non-specific response involves various physical, chemical and cellular factors coming into play when a pathogenic invasion is detected. Studies have shown that probiotics caused an elevated production of leucocytes, phagocytes, granulocytes, erythrocytes, etc which are nothing but the cellular components released as a response to infection [79] for example, *Labeo rohita* showed enhanced immune parameters when fed with a probiotic *Bacillus subtilis* [80]. Hence, probiotics are not only capable of inhibiting pathogens but also increase immunity of the host against infections. Probiotics possess certain structures such as peptidoglycan (PGN), exopolysaccharides (EPS), S-layer protein A (SlpA), lipoteichoic acids (LTA), flagellin and microbial nucleic acids and also the conserved microbe-associated molecular patterns (MAMPs) which are capable of being recognised by pattern recognition receptors (PRRs) which in turn produce effector molecules such as cytokines, chemokines, and others [81]. Apart from phagocytic activity, elevating the production of antibodies, lysozymes, acid phosphates, gamma interferons, antimicrobial peptides are some of the actions often found in fishes fed with probiotics [82] [83]. They also helped in producing inhibitory compounds such as sideropheres, bacteriocins, proteases, lysozymes, hydrogen peroxides, increase production of digestive enzymes like amylase, protease and lipase and their activity, and by producing vitamins, fatty acids, and essential amino acids that are useful for lactic acid bacteria could improve the growth performance [84] [85]. Apart from this, they also play a role in modulating the gut immune system. Studies have shown that probiotics are capable of enhancing the f IgC-cells and acidophilic granulocytes (AGs) in fishes [86]. For example, a study showed that the intraepithelial lymphocytes were significantly higher in the probiotic supplemented group than in the control group of Nile Tilapia [87].

Production of inhibitory chemicals- Probiotics are capable of conferring anti pathogenic properties to its host by producing a large number of inhibitory molecules such as bacteriocins, hydrogen peroxide, acetoin, diacetyl, lysozymes and siderophores [88]. Bacteriocins are ribosomal peptides with great capacity to fight against pathogens. Also, a study suggested that a probiotic strain of Aeromonas produced extracellular bactericidal substances which was later identified to be indole (2,3 benzopyrrole) by Nuclear Magnetic Resonance (NMR) scan [89]. The capacity of probiotic bacteria to produce bactericidal substances such as antiprotease, lysozyme, serum peroxidase enables its use as an effective alternative to antibiotics [90]. Probiotic strains of *Bacillus licheniformis* and *B. pumilus* which survived low pH and high bile concentrations were able to produce antibacterial substances in a study [91]. In addition to antibacterial activity, few studies have also shown how probiotics elicit antiviral response against hematopoietic necrosis virus (IHNV) in salmonid hatcheries [92] and antifungal activity against saprolegniosis, a fungal disease caused by *Saprolegnia ferax* in eels [93].

Competition for space and energy- Most of the pathogenic bacteria require adherence on the mucosal epithelium of gastrointestinal tract of their hosts to be able to effectively take in nutrients and colonise [94]. Probiotic strains of bacteria are also found to adhere and colonise in the same surface which reduces the availability of space for the pathogenic microorganisms. This is called competitive exclusion [95]. The GI epithelium has different surface receptors or determinants which are available for interaction with different bacterial species including pathogenic ones, but probiotics being more competitive adhere more easily leaving no space for pathogens [96]. In fact, a study suggested that competition for space along with nutrients is the way by which probiotics offer protection to their host [97]. Their attachment to host epithelium may be specific or non-specific based on various physicochemical agents and also the kind of receptors present in the host gut that is available for binding [98]. One study suggested the competition for iron between pathogenic bacteria and probiotic bacteria. Specific iron binding agents called siderophores are needed for the bacteria for their efficient uptake of iron from the host and survive. Due to presence of probiotics, there is limited availability of iron for uptake by pathogenic bacteria [99].

Enhancing the quality of water- The conversion of organic compounds to carbon dioxide by Gram positive bacteria is efficacious than Gram negative bacteria [99] Since *Bacilli* are Gram positive, enriching water with these organisms can reduce build-up of organic matter, eventually increasing survival and growth rate of shrimps [101]. In addition, presence of probiotics in water increases the load of good microbes and the water conditions such as the pH, temperature, dissolved ammonia and oxygen, etc thereby improving the growth and survival of shrimps and prawns [102].

7. SIDE EFFECTS

Probiotic application is generally considered safe but in certain instances they are capable of showing side effects. Probiotic microorganisms can sometimes move from the target site i.e., the gastrointestinal site to other parts and cause systemic infections [103]. Also, introduction of probiotics in importation in the aquaculture industry, can possibly change intestinal microflora giving rise to diseases, mutagenesis or recombination of DNA of bacteria which may result into systemic infections and economical losses [104].

8. CONCLUSION AND FUTURE STUDIES

Despite having done a lot of research on efficiency and mechanisms of probiotics, there are many questions that remain unanswered. Future studies can be directed towards transcriptome and proteome profiling of gut microbiota, interactions between gut microbes, the intestinal epithelium, gut immune system, antioxidant status, host lipid levels, antagonistic and synergist activity and probability of side effects of probiotics.

Aquaculture holds an important place among the fastest developing industries globally and contributes about 90% of the world production. It is an important source of fishes with ample nutritional profile for human consumption but are still susceptible to infections, disease outbreaks in large aquaculture industry which can not only affect socio-economic status but also economic advancement of the country as a whole.

An interactive discussion among world academicians, scientists, producers and owners of aquaculture industry is required to focus and explore the different aspects of bacteria host interactions conferring the possible favourable changes in diverse immune responses elicited by different bacterial strains in order to propose clinically effective, bacteria-based strategies to promote the health, production and economic growth of the aquaculture industry.

They should not be treated as a magical potion, rather they should be used as supplement to maintain a balanced diet to avail for an overall healthy profile which is free from infections and disease-causing microorganisms. The present review has summarized some of the important probiotics, their use and their future perspectives in fastest growing food production sector of aquaculture industry.

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