Alternative to antibiotics in aquaculture practices

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Introduction

Antibiotic resistance has grown and spread as a result of the extensive and regular use of antibiotics in aquaculture. Antibiotics are being used by fish farmers to combat sickness in aquatic animals with the same antibiotics that humans use to treat illnesses, for therapeutic purposes. Afterwards, it was discovered that they could promote growth *i.e.*, they were shown to be capable of supporting growth. According to previous scientific data, antibiotic usage in food-producing animals can cause intestinal bacteria to become resistant to the drugs, which can subsequently be spread to the general population and result in diseases that are difficult to treat. These antibiotic applications can also lead to the development of antibiotic resistance in non-pathogenic bacteria, whose resistance genes can then be passed on to pathogenic bacteria, resulting in human illnesses that are resistant to antibiotic treatment. So, the application of antibiotics can be reduced by various alternative materials.

Probiotics

Probiotics are living microorganisms that are supposed to benefit the host's health by introducing beneficial bacteria into the stomach. Probiotic species studied in aquaculture include *Lactobacillus*, *Bacillus*, *Enterococcus*, *Carnobacterium*, *Saccharomyces*, and *Candida*. There are essentially two types of probiotics *i.e.* Water probiotics can grow in a water medium and exclude harmful bacteria by absorbing all available resources. Gut probiotics can be mixed with feed and administered orally to enhance the beneficial microbial flora of the gut, thus, malnutrition causes harmful bacteria to die (Sahu et al., 2008). Probiotics have been proven to protect rainbow trout from bacterial illnesses caused by *Vibrio, Aeromonas, Yersinia*, and *Ichthyophthirius*. In addition, *Lactobacillus* improved fish health, survival, and growth performance in African catfish. *Bacillus* bacteria were demonstrated to boost the survival of pond-raised catfish. These organisms are either directly put into the fish's aquatic habitat or delivered orally as feed. Probiotics are crucial in the degradation of organic waste, which considerably lowers the production of sludge and slime. By lowering the occurrences of diseases (including *Vibrio sp.*, *Aeromonas sp*., and viruses), the water quality will consequently improve the zooplankton populations, minimizing odours, and eventually increasing aquaculture output.

Prebiotics

A prebiotic is a substance considered to benefit the host by encouraging the development or activity of naturally occurring bacteria in the gastrointestinal system *E.g.*, fructooligosaccharides, galactooligosaccharides, and mannan-oligosaccharides, dextrins, inulin, lignin, waxes, beta-glucans. Many different types of prebiotics have been fed to various fish species, with diverse results E.g. Inulin has recently been found to modify the intestinal microbial populations of turbot, Arctic char, Atlantic salmon, and hybrid striped bass. Prebiotics such as glucans has been proven to protect channel catfish from enteric septicemia when injected but not when fed. Furthermore, a prebiotic made up of brewer's yeast, dairy

components, and dried fermentation products were discovered to greatly improve feed efficiency and minimize mortality in hybrid striped bass challenged with bacterial infections.

Synbiotics

Synbiotic is a combination of prebiotics with probiotics. Synbiotics may function by encouraging the growth of helpful bacteria in the host's gastrointestinal system. There are no studies in aquatic animals that have investigated the efficacy of these products, although synbiotics can manipulate gut microbiota and improve growth and disease resistance.

Bacteriophage

Bacteriophages are viruses that can infect, proliferate, and kill vulnerable bacteria. They are both pervasive and plentiful in the environment, particularly in saltwater, where the total number of viruses frequently surpasses the bacterial concentration by a factor of ten. Phages have been examined for their medicinal characteristics and capacity to control pathogenic germs since their discovery in 1915; however, these studies were eventually abandoned due to the emergence of cheap, broad-spectrum antibiotics. Following the rise of bacterial drug resistance, phage treatment has recently resurfaced as a viable alternative to the usage of antibiotics.

Bacteriocins

Bacteriocins are substances having an essential biological protein moiety that possesses a bactericidal mode of action against other bacteria. It is one of the immunity mechanisms of bacteria that protects from other bacteria *i.e.*, bacteriocins may serve as anti-competitor compounds to protect the own microbial community. The advantages of bacteriocin are nontoxic and non-antigenic to animals including humans; moreover, it is easily degraded by proteolytic enzymes of the gastrointestinal tract; hence, it can be incorporated into the feed. The role of bacteriocins in microbial communities hasn't been well-established yet. Since the use of prophylactic antibiotics is detrimental to aquatic and terrestrial environments, the application of bacteriocinogenic bacterial strains appears to be an excellent candidate for a friendly alternative.

Essential Oils

Compounds formed during plant secondary metabolism are found in essential oils, they are intricate combinations of low-molecular-weight compounds with a wide range of chemical characteristics. Some EOs can reduce oxidative stress when added to therapeutic baths (at doses lower than those that cause drowsiness). For instance, the essential oil of Melaleuca alternifolia might stop the effects of disease-induced splenic pyruvate kinase and creatine kinase inhibition. It is understood that several EOs control GABA, the primary inhibitory neurotransmitter in the CNS, to produce their anesthetic effects.

Organic Acids

The application of the organic acid would lower the pH (around 3.5) of the environment, which provides a favorable environment for the proliferation of beneficial bacteria. E.g. *Lactobacillus* can proliferate in acidic conditions. Most of the pathogenic bacteria such as *V. parahaemolyticus* and *V. cholera* would die in acidic condition. Various kinds of researches were carried out in the laboratory and found that the organic acids are highly efficient to control all pathogenic vibrio. The mechanism of action is mostly based on the lower pH. Since *Vibrio sp.* prefer to grow in alkaline condition, *Vibrio sp.* are highly susceptible to the short chain organic acid.

Antimicrobial Peptides

Antimicrobial peptides (AMP) are called host defence peptides and are responsible for the innate defined mechanism produced by the host cell to destroy the invading bacteria/viruses. It is well developed in fish and shellfish. Antimicrobial components are made up of short chain of amino acids *i.e.*, between 12 to 15 amino acids. Since these molecules are short-chain, they generally are thermostable. Recently, these antimicrobial peptides are considered as a novel substance as an alternative to antibiotics owing to their ability to kill the target organism with a broad range of bactericidal activity, e.g., Pleurocidin from winter flounder, cathelicidins from rainbow trout, defensins from zebrafish, piscidins from hybrid striped bass, dicentracin from sea bass, hepcidin from channel catfish and epinician from the groupers.

Plant compounds with antimicrobial activity

Numerous research has been carried out regarding the application of plant extract for the treatment of infection in humans as well as preservative materials for shelf-life extension of food materials. Most plant extracts are having excellent antimicrobial activity, but limited research has been carried out on the application of plant materials to aquaculture practices. Well-characterized plant materials can be tried in aquaculture practices. But the materials should be available regularly, capable of showing significant improvement for disease control, and should not have any negative effect on the fish/ shrimps as well as consumers.

Nanoparticles

Nanoparticles possess potential antibacterial activity; especially metal nanoparticles are highly active against a wide variety of microorganisms on multi-drug-resistant bacteria. The application of silver nanoparticles is able to control the MDR in aquaculture, but the application is highly restricted. Hence, a suitable substance needs to be investigated to reduce the toxicity of the nanoparticles for application in aquaculture.

Seaweed Extracts

Extract of seaweed *viz.*, *Ascophyllum nodosum* causes a better immune system to combat most threatening diseases. India is having a wide range of marine resources with various unexplored seaweed materials. So, it is a potential area to identify suitable seaweed material for aquaculture practices. FAO also suggested that research can be taken to explore the benefit of aquaculture species.

Competitive Exclusion (Nurmi Effect)

Competitive Exclusion is otherwise called as Nurmi Effect. In 1973, Nurmi and Rantala introduced a new technique in poultry to get rid of resistant and pathogenic bacteria. They collected intestinal gut microbes/faecal materials from the healthy birds and fed them to newly hatched chicks to establish a healthy bacterial population in the intestine. This technique was similar to the probiotics, but it will be applied to the newly hatched chicks. The Nurmi effect was tried in the Tilapia aquaculture form and found a greater effect on the pathogens.

Anti-Virulence Therapy

Anti-virulence therapy is either interfering with the control of virulence factor expression or particularly suppressing a particular virulence. Many Gram-negative bacteria produce i.e., N-acyl homoserine lactones (AHLs) as signal molecules, which favours biofilm formation. But, in the case of Vibrios species, various chemicals i.e., multichannel quorum

sensing mechanisms responsible for the biofilm formation. The substance exhibits quorum quenching properties and may be used as a replacement for antibiotics.

Vaccination

Although vaccination is the best way to avoid infectious illnesses, it is not a cure for already existing infections, and there are still relatively few commercially accessible vaccinations for the aquaculture industry. Autogenous immunization has advantages for animal welfare, transboundary biosecurity, local farmer and industry economics, and public health, which favour its use in aquaculture as a locally enabled response to the widespread issue of antimicrobial resistance. To produce 1,375,307 tonnes of fish in 2019, the Norwegian salmon industry utilized 222 kg of antimicrobials (160 mg antimicrobial per tonne). The development of vaccination against the main bacterial illnesses allowed for the shift from treating to preventing disease in farmed fish. Aquaculture also employs auto-vaccines, which have shown success against atypical *Aeromonas*, new *Yersinia ruckeri* biotypes, infections in salmonids, Streptococcal diseases in barramundi and stingrays, and others. Autogenous vaccinations against the intracellular pathogen Francisella noatuensis have been demonstrated to be efficacious in Tilapia. The variety of sizes of the sectors is reflected in Australia's usage of licensed and autogenous vaccines in the finfish aquaculture industry.

Immunologically-Active Compounds

A variety of immunologically active compounds are available in the market such as cytokines, freeze-dried eggs, spray-dried plasma, and antibodies. Research needs to be carried out on the effect of this product on aquaculture species. Most of the immunostimulants are obtained from either bacteria or red and brown algal groups. Since fish and shellfishes are devoid of acquired immunity, immunologically active components are needed in the aquaculture species to withstand the disease outbreak; which is indirectly useful to reduce the usage of antibiotics in the aquaculture system.

Hygienic Procedure

The use of antibiotics can be greatly reduced if proper health management practices are adopted. So, good aquaculture practices are a highly efficient way to produce an antibiotic-free environment. Office International des Epizooties (OIE) has given clear guidelines for good aquaculture practices.