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Antibiotic Use in Aquaculture and Their Impact on the Aquatic Environment

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Abstract

The rapid expansion of aquaculture through the intensification method has promoted numerous bacterial diseases which require the intensive use of antimicrobials. These compounds are mainly used for therapeutic, prophylactic, or metaphylactic in aquaculture meanwhile there are no antibiotics particularly designed for aquaculture and these compounds are authorized products used only for veterinary medicine. However, the frequent use of antibiotics in aquaculture has produced negative impacts including the development and spread of antimicrobial resistant bacteria and resistance genes and the presence of antimicrobial residues in aquaculture products and the environment. Antimicrobial resistance (AMR) is a major threat in aquaculture that has to be prevented by continuous monitoring programs such as proper guidelines, legislations and effective policies then have to be effectively followed by alternative strategies such as probiotics, vaccination, and herbal medicines. This article highlights the use of antimicrobials in aquaculture and their impacts in aquatic animal, human and aquatic environment.

Introduction

Aquaculture plays an important role in food production sectors worldwide which contributes 8% of animal food protein intake to the human diet that also provides raw materials for industrial and pharmaceutical use, and aquatic organisms for stocking or ornamental trade have increased dramatically in recent decades. Aquaculture has rapidly developed due to intensified culture methods. Intensification and commercialization of aquaculture production are mainly affected by several factors such as combating diseases and epizootics, brood stock improvement and domestication, development of appropriate feedstuffs and feeding mechanisms, hatchery and growout technology as well as water quality management. However, the current intensification of aquaculture has led to significant damage to the environment due to discharges of concentrated organic wastes, depleting dissolved oxygen in ponds, giving rise to toxic metabolites of hydrogen sulfide, methane, ammonia, and nitrites. These conditions are led to the promotion of conditions that favor the development of infection and disease-related problems. The disease is recognized as one of the major threats to sustainable aquaculture production which can cause significant economic loss due to mortality and morbidity, poor growth rate, low quality of flesh, or reduced trade in aquaculture. Various chemotherapeutic agents such as antibiotics and disinfectants have been commonly used in the treatment and prevention of numerous infectious diseases in farmed fish and shrimp. In aquaculture, antibiotics are generally administered by oral (surface-coated or pelleted feeds), immersion and injection methods.

Use of Antimicrobial in Aquaculture

Diseases are a major constraint to aquaculture production and it is caused by virus, bacteria, fungi, and parasites. Among these commonly bacterial pathogens are cause the major impacts in aquaculture production. For examples of Gram-negative organisms such as *Aeromonas hydrophila, A. salmonicida, Vibrio anguillarum, V. harveyi, Flavobacterium psychrophilum, Edwardsiella tarda, Citrobacter freundii, Pseudomonas fluorescens* and *Yersinia ruckeri*, rarely by Gram positive *Streptococcus* and *Staphylococcus* and also by acid-fast *Mycobacterium* sp. In this group, *Aeromonas hydrophila* has been reported as an opportunistic pathogen in freshwater aquaculture. The consumption of *Aeromonas hydrophila* infected cultured fishes have public health concerns including humans. This incidence and other bacterial diseases induce the farmers to use antibiotics frequently in the aquaculture system.

Many antimicrobials compounds are used in aquaculture and food animals, these compounds are also used in human medicine which is characterized as therapeutic, prophylactic, or metaphylactic based on usage. Antibiotics acts as therapeutic, be regularly administrated for short periods of time through oral route to a group of fish culture in tanks or cages. In aquaculture use of all groups of antibiotics should be legally approved by Food and Drug Administration (FDA) in the USA is a government organization mainly responsible for the use of veterinary medicine.

These agencies give a guideline or rules for use of antibiotics in food animals which include dosage, routes of delivery, withdrawal times, tolerances, and use by species as well as dose rates and limitations. Antibiotics are used in aquaculture which is classified into different groups based on the chemical structure that includes aminoglycosides (AGs), quinolones (QNs), sulfonamides (SAs), tetracyclines (TCs), macrolides (MLs), chloramphenicols (CAPs), β-lactams, nitrofurans (NFs), lincosamides (LINs), polymyxins (PLs) and some others (Table 1). Antibiotics further divided into natural antibiotics (*e.g.*, erythromycin, oxytetracycline, tetracycline, and chloramphenicol) and semi synthetic antibiotics (*e.g.*, most of β lactams), synthetic antibiotics (*e.g.*, quinolones, nitrofurans, and florfenicol) and other chemically modified derivatives (*e.g.*, oritavancin, telavancin, and ivermectin). These semi synthetic antibiotics, synthetic antibiotics and other chemically modified derivatives have been gradually replaced by the natural antibiotics in aquaculture. Moreover, some of the following antibiotics are used for different fields such as veterinary (*e.g.*, enrofloxacin and florfenicol), human (*e.g.*, chloramphenicol, erythromycin, and ciprofloxacin), as well as some antibiotics, are used for both aquaculture and human.

Table 1: Antimicrobial resistant bacterial pathogens associated with cultured fishes and crustaceans (Preena *et al*., 2020)

Sl. No.	Species	Organism	Resistant antibiotics	Place
1.	Cultured catfish	*Aeromonas hydrophila* and *Plesiomonas shigelloides*	Tetracycline, oxytetracycline, chloramphenicol, kanamycin, ampicillin, and nitrofurantoin	United States
2.	Gold fish and Koi	*Aeromonas* sp.	Multiple antibiotics	United States
3.	Diseased penaeid cultured shrimps	*Vibrio harveyi*	Erythtromycin, gentamycin, ampicillin, polymyxin B, oxytetracycline, novobiocin, rifampicin, chlorotetracycline, streptomycin, ceprofloxacin, penicillinG, furazolidone, nalidixic acid and neomycin	India
4.	Rainbow trout farms	*Aeromonas*, *Flavobacterium*, *psychrophilum* and *Yersinia ruckeri*	Multiple antibiotics	Denmark
5.	Rainbow trout farms	*Aeromonas* sp.	Oxytetracycline and sulphadiazine/ trimethoprim	Denmark
6.	Pond cultured shrimps	*Vibrio harveyi*	Oxytetracycline, oxolinic acid, chloramphenicol, furazolidone	Philippines
7.	Cultured yellowtail fishes	*Vibrio* sp.	Oxytetracycline	Japan
8.	Salmon fish farms	Moraxella	Tetracycline	Chile
9.	Cultured Fish farms	*Photobacterium, Vibrio*, *Pseudomonas*, *Alteromonas*	Tetracycline	Japan

Table 1: Continue...

Sl. No.	Species	Organism	Resistant antibiotics	Place
10.	Marine aquaculture site	*Vibrio* sp., *Lactococcus garviege*, *Photobacterium damsel* subsp. *piscicida*	Tetracycline	Japan and Korea
11.	Freshwater trout farms	Acinetobacter	Tetracycline	Denmark
12.	Freshwater ornamental fishes	*Aeromonas* sp.	Ceftazidime, chloramphenicol, ciprofloxacin and gentamicin	India
13.	Farmed fish and crustaceans	*Vibrio* sp. and *Aeromonas* sp.	Ampicillin, amoxycillin, cephalexin, erythromycin oxytetracycline, tetracycline, nalidixic acid, sulfonamides chloramphenicol, florfenicol, ceftiofur, cephalothin, cefoperazone, oxolinic acid, gentamicin, kanamycin and trimethoprim	Australia
14.	Tilapia, trout and koi	*Aeromonas salmonicida* and *A. hydrophila*	Tetracycline and amoxycillin	South Africa
15.	Cultured fishes	*Photobacterium damselae*	Kanamycin, chloramphenicol, tetracycline, and sulfonamide	Japan and United States
16.	Abalone and turbot from mariculture farms	*Vibrio splendidus, Vibrio tasmaniensis, Pseudoalteromonas marina, Mucus bacterium, Pseudoalteromonas haloplanktis*	Oxytetracycline, streptomycin, chloramphenicol, ampicillin, nalidixic acid	China
17.	Fish farms	*Acinetobacter* sp.	Tetracycline and sulphonamides	Thailand
18.	Trout from mariculture farms	*Edwardsiella tarda*	Chloramphenicol	China
19.	Ornamental fishes and carriage water	*Aeromonas* sp.	Tetracyclines, fluoroquinolones and betalactams	United Kingdom
20.	Freshwater Carp	Enterobacteriaceae and *Flavobacterium* sp.	Oxytetracycline	India
21.	Cichlid & Oscar	*Aeromonas veronii*	Multiple antibiotics	India
22.	Marine shrimps	*Vibrio* sp.	Ampicillin and tetracycline	Brazil
23.	Fish farms	Enterobacteriaceae	Tetracyclines	Chinese
24.	Atlantic salmon and brown trout	*Flavobacterium psychrophilum*	Quinolones	Norway
25.	Salmon aquaculture	*Vibrio* sp.	Tetracycline, quinolones	Chile
26.	Tropical ornamental fish	*Aeromonas hydrophila*	Quinolones, sulphonamides, tetracycline	Czech Republic
27.	Freshwater ornamental fish	*Aeromonas dhakensis*	Tetracycline and erythromycin	Sri Lanka
28.	Cultured Rainbow trout	*Aeromonas* sp.	β lactam antibiotics	Mexico

Table 1: Continue...

Sl. No.	Species	Organism	Resistant antibiotics	Place
29.	Salmon aquaculture	*Bacillus aryabhattai, Exiguobacterium sibiricum, Marinobacter litoralis, Psychrobacter pulmonis, Stenotrophomonas maltophilia, Thalassospiro xiamenensis*	Tetracycline and sulphonamides	Chile
30.	Yellow swordtails and freshwater fishes	*A. hydrophila, A. allosaccharophila, A. veronii, A. sobria, A. caviae* and *A. media*	Quinolones	South Africa
31.	Aquaculture farms	*Aeromonas* sp.	Multiple antibiotics	China
32.	Diseased cultured gilthead sea bream	*Pseudomonas aeruginosa*	Tetracycline, ampicillin and erythromycin	Africa
33.	Cultured Cobia, mullet and loach	*Streptococcus dysgalactiae*	Macrolide and tetracycline	Taiwan and Japan
34.	Aquaculture fish	*Pseudomonas, Chryseobacterium*, Enterobacteriaceae and *Aeromonas* sp.	β lactams	Europe

Impacts of Antimicrobial Residues in Aquaculture and Human Health

Antibiotics have the potential to inhibit growth or kill pathogenic bacteria by disrupting cell membranes, disrupting protein or DNA synthesis, and inhibiting enzyme activity. The use of antimicrobial in food animals including aquaculture is increasing enormously, estimated at 63,151 tons in 2010 and expected to rise by 67% in 2030 worldwide. Especially some countries such as Brazil, Russia, India, and South Africa are considered to have the highest estimated global antimicrobial consumption. The constant and enormous use of antibiotics in the aquaculture system could lead to various hazards to the health of aquatic organisms as well as to humans on the consumption of aquatic culture animals. The significant use of antibiotics in aquatic cultured animals are the presence of drug residues, even in very low concentrations, in the edible tissues of the treated animal.

Antibiotics are administrated to cultured aquatic animals through formulated feed mixing with these compounds by oral routes. However, fish are not able to efficiently or properly metabolize the antibiotics and these compounds are as an unused form back into the culture environment through feces (estimated that 75% of the antibiotics fed to fish are excreted into the water).

The use of antibiotics in aquaculture based on label directions should not result in residues at slaughter. The presence of antibiotics residue in edible tissues of aquatic cultured animals include the following reasons non-adherence to recommended label directions or dosage (extra-label usage), non-observance of recommended withdrawal periods, administration of too large a volume at a single injection site, use of antibiotic-contaminated equipment or failure to properly clean equipment used to mix or administer drugs mixing errors, unintentional feeding with spilled chemicals or medicated feeds, animal effects such as age, breeding period, congenital, illness, and allergies, chemical interactions between drugs, variations in water temperature for aquatic species, environmental contamination and improper use of drugs (Figure 1).

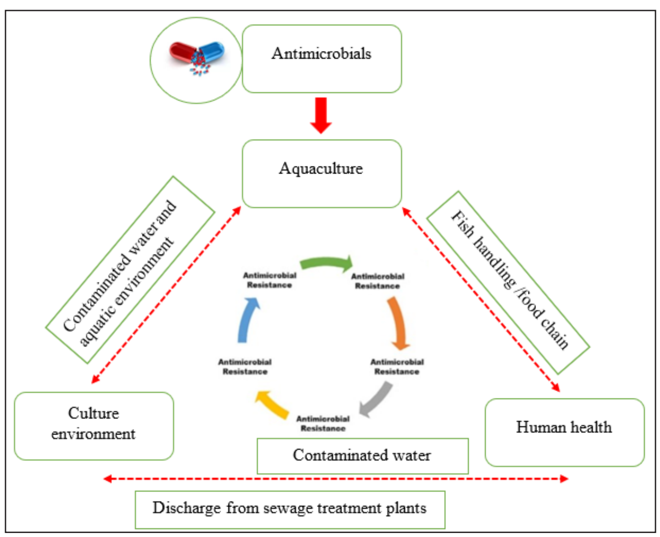

Figure 1: Drivers of antimicrobial resistance related to the use of antimicrobials in aquaculture (Source: Santos and Ramos, 2018)

For these reasons, in aquaculture, the use of antibiotics has been banned by the marine products export development authority of India those compounds are Chloramphenicol, Nitrofurans, Neomycin, Nalidixic acid, Sulphamethoxazole, Aristolochia, Chlorprpmazine, Colchicine, Apsone, Dimetridazole, Metronidazole, Onidazole, Ipronidazole, Nitroimidazoles, Clenbuterol, Diethylstilbestrol, Sulfonamide, Floroquinolones, and Glycopeptides. In fish and shrimp aquaculture irrespective of the route or purpose of administration and extra-label usage leads antimicrobials residues to accumulate in tissues before they are completely metabolized or excreted from the body. Likewise, a most important concern is the occurrence of antimicrobials residues in fish or other animal tissues is most likely when animals are harvested for human consumption while still on medication or shortly after medication before the withdrawal period elapses. During consumption of such products of antibiotics lead to many health problems in humans due to the withdrawal of antibiotics from the fish body during harvesting.

Antimicrobial Resistance

Recently emergence of antimicrobial resistance (AMR) in cultured shrimp and fishes is one of the most important tasks faced in aquaculture. The frequent occurrence of bacterial infections in both fish and shrimp farming has promoted the intensive use of antibiotics and their persistence in the culture environment which leads to the proliferation of antibiotic-resistant bacteria. Moreover, the AMR in aquaculture can be transferred to clinically significant bacterial strains of the natural environment by horizontal gene transfer, thus disturbing the whole ecosystem.

However, human life is in direct and intimate contact with the aquatic environment because it is providing fish and shrimp food for consumption. Antibiotic resistance causes a threat to public health and ecosystems due to the consumption of food animals from aquaculture. Moreover, the use of antibiotics in aquaculture is non-biodegradable and remains in the aquaculture environment for long periods of time. This characteristic of antibiotics encourages the growth of bacteria that can survive in the aquatic environment even presence of antibiotics and also acquiring a resistance that is passed on to consequent generations. These bacteria transfer to animal and human pathogens which lead to increased infectious disease in fish, animals, and humans alike.

Management Measures to Reduce the Need and Prudent Use of Antibiotics in Aquaculture (Okocha *et al.*, 2018)

- The requirement for antibiotics in aquaculture should be reduced by improving aquatic animal health by the implementation of bio-security measures, disease prevention, good hygiene and management practices.
- Antibiotics should be used for the aquatic cultured animals after being prescribed by veterinarian or fish pharmacologist.
- Antibiotics should be used in aquatic food animals therapeutically and based on the results of resistance surveillance as well as clinical experience.
- Use of antibiotics should be avoided as a growth promoter in cultured animals.
- Selected antibiotics should be characteristics of narrow-spectrum for therapy in aquaculture.
- Before usage of antibiotics in aquatic cultured animals should be identified whether this same group of antibiotics used as medicine for infectious diseases in humans.
- The recommend/approved level of antibiotics should be used on food animals for treatment.
- Use of antibiotics in aquaculture should be based on international guidelines, adapted to countries circumstances as well as followed at the national level.
- Use of antibiotics in aquaculture encourage by economic incentives that should be eliminated which lead to the use of inappropriate prescription of antibiotics.
- During preparing or administering antibiotics for the treatment of diseases, farmworkers should use protective measures like wearing gloves and mask it prevents unnecessary exposure.
- Avoid the use of antibiotics after the expiration date or stored in the proper place to store in hot and humid conditions that reduced efficacy as well as cause toxic effect.

Conclusion

Antibiotics are used as chemotherapeutic agents for the treatment of bacterial infectious diseases in aquaculture and there can be characterized as therapeutic, prophylactic or metaphylactic based on usage. Moreover, the rise of production and demand for aquaculture products worldwide has promoted the intensive use of antimicrobial compounds that also leads to the presence of residues in the products produced for human consumption. Although, the administration of antibiotics in aquatic food animals has been uncontrolled in many countries due to weak regulations, poor management practices, and the spreading of emerging diseases. The complexity of antimicrobial resistance in aquaculture can be unravelled by a detailed understanding of the gene transfer systems such as plasmids, transposons, integrons, and gene cassettes. Recently antimicrobial resistance is one of the major threats in aquaculture that have to be controlled by the implementation of continuous monitoring programs such as proper guidelines, effective policies, evaluation of antibiotic residues, identification of responsible pathogens, and determination of their antimicrobial susceptibilities. However, several alternative strategies to antibiotics have been developed including probiotics, phage therapy, vaccination, implementation of best management practices, and disease monitoring as well as herbal medicine and some of these have been successfully used to control bacterial infections in fish and shrimp aquaculture.

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