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EDITED BY
Ankures Bhattacharya
West Bengal University of Animal and Fishery Sciences

REVIEWED BY
Dr. Prasenjit Mali
West Bengal University of Animal and Fishery Sciences

Dr. Swarnadyuti Nath
West Bengal University of Animal and Fishery Sciences

*CORRESPONDENCE
Ishwar Chandra
ishwar8576042433@gmail.com

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Application of Antibiotics in Aquaculture: Effects on Aquatic Life and Human Health

Ishwar Chandra[1], Durgesh Kumar Verma[2], Narendra Kumar Maurya[3], Ajay Kumar Verma[4] and Rajesh Jaiswal[2]

[1]Faculty of Fisheries Science, Kerala University of Fisheries and Ocean Studies, Kochi, Kerala (682 506), India.
[2]ICAR-CIFRI, Regional Centre, Allahabad, Uttar Pradesh (211 002), India.
[3]College of Fisheries, Mangalore, Karnataka Veterinary, Animal and Fisheries Sciences, University, Bidar, Karnataka (575 002), India.
[4]College of Fisheries Science, CCSHAU, Hisar (12504), India.

The rapid expansion of aquaculture has resulted in several developments that are harmful to human and aquatic animal health, as well as the environment. People use various prophylactic antibiotics indiscriminately in aquaculture, primarily in developing countries, to prevent various bacterial infections caused by sanitary flaws in fish and shellfish farming. Furthermore, the use of a wide range of non-biodegradable human antibiotics remains in the aquatic environment. It directly causes antibiotic-resistant bacteria to develop, and transferable resistance genes can be transferred to disease-causing bacteria, resulting in antibiotic-resistant infections in humans, fish, and other aquatic animals. The more antibiotics that are used, the more likely it is that antibiotic-resistant bacteria will win the battle for the survival of the fittest at the bacterial level. The presence of antibiotic compounds in terrestrial and aquatic environments is of greater interest worldwide due to their emergence as dangerous pollutants for the environment and human health.

Keywords
Aquaculture, Antibiotics, Antibiotic Resistance and Aquatic Animal Health

Introduction

Aquaculture is becoming a more concentrated industry, with fewer but much larger farms. Infectious diseases are always a risk and can result in significant stock losses as well as animal welfare issues. Intensive aquaculture (shrimp and fish farming) has resulted in an increase in Antimicrobials that are now being extensively used to treat bacterial diseases. Although several authors have emphasized the potential negative effects of using antimicrobial agents in fish farms, few in-depth studies on antimicrobial resistance in the aquaculture industry have been conducted. Over the years, various measures have been implemented. These include disinfectants (such as hydrogen peroxide and malachite green), antibiotics (such as sulfonamides and tetracyclines), and anthelmintic agents, such as pyrethroid insecticides and environmental disease control is an active research field, and alternatives to antibiotic treatments have been investigated (Romero *et al.*, 2012).

Antibiotic use in aquaculture

Antimicrobial agents are substances with the ability to kill or inhibit the growth of microorganisms. Natural or synthetic antibiotics should be safe for the host, allowing them to be used as chemotherapeutic agents in the treatment of infectious diseases. Antibiotics are given to fish in the form of food, baths, and injections. Unconsumed food and antibiotic-containing fish faces spread the sediment at the bottom of the raising put antibiotics are leaches (Rasul and Majumdar, 2017).

Table -1: Antibiotic use in Indian aquaculture

Antibiotic	Treatment	Mode of application
oxytetracycline	*Myxobolus* spp.	Supplemented in feed
Sulfadiazine + trimethoprim	Ulcerative and systemic type (*Aeromonas hydrophila*)	Water dispersible powder
chlor-tetracycline	Not Defined	Supplemented in feed
oxytetracycline	Columnaris disease	Supplemented in feed

Source: Serrano (2005)

Table -2: Antibiotic use in Indonesian aquaculture

Antibiotics	Treatment	Mode of application
Oxytetracycline	bacterial fish and shrimp disease	bath and oral
chloramphenicol	bacterial disease in shrimp and ornamental fish	immersion
Erythromycin	bacterial fish and shrimp disease	bath
Streptomycin	bacterial disease in shrimp and ornamental fish	long bath
Neomycin	bacterial disease in shrimp and ornamental fish	bath

Source: Serrano (2005)

NOTES: Negative effects: the antibiotic application has resulted in the emergence of drug-resistant bacteria, and the detection of antibiotic residues in exported fish products has resulted in rejection by the Japanese market. List of antibiotics and pharmacologically active substances banned by MPEDA that are used in Indian aquaculture. Through (MPEDA) is given in Table 3.

Table-3: List of banned antibiotics and Pharmacology active substances

1	Chloramphenicol	11	Dimetridazole
2	Nitrofurans	12	Metronidazole
3	Neomycin	13	Onidazole
4	NalidixicAcid	14	Ipronidazole
5	Sulphamethoxazole	15	Nitroimidazoles
6	Aristolochia	16	Clenbuterol
7	Chlorprpmazine	17	Diethylstilbestrol
8	Colchicine	18	Sulfonamide
9	Apsone	19	Floroquinolones
10	Chloroform	20	Glycopeptides

Source: Vignesh et. al., (2011)

Antibiotics: Mechanisms of Action

Antimicrobial drugs can have a variety of chemical structures and target different parts of bacterial machinery. Antibiotics generally work through one of two mechanisms.

1. A bactericidal effect, which means that the antibiotic kills bacteria by interfering with the formation of the bacterium's cell wall or its cell contents. Penicillin, fluoroquinolones, and metronidazole are few examples.
2. A bacteriostatic effect, which means that the antibiotic inhibits bacterial growth by interfering with bacterial protein production, DNA replication, or other aspects of bacterial cellular metabolism. Tetracyclines, sulfonamides, chloramphenicol, and macrolides are some examples (Romero *et al.,* 2012).

Resistance mechanisms and transference

Antimicrobial drug use in aquaculture differs significantly from that of terrestrial animals. Antimicrobials are regularly added to aquaculture feed, which is then placed in the water where the fish are kept. Several bacterial species may survive in unfavorable conditions or environmental changes if mutations that improve their fitness in the new conditions are selected. Some of these genes may provide resistance to antibiotic effects.

1. Inherent or intrinsic resistance, which means that the species is not normally susceptible to a specific drug. This could be due to the antibacterial agent's inability to enter the bacteria cell and reach its target site, a lack of affinity between the antibacterial and its target site of action, or the cell's lack of the target. It has been proposed that some bacteria are naturally resistant to entire classes of antimicrobial agents. In such cases, all strains of that bacterial species are resistant to all antibacterial class members.
2. Acquired resistance developed. Because of the transmissible nature of the resistance mechanisms, this type of resistance is the most concerning. The bacterial species in this case is normally susceptible to a specific drug, but some strains express it. Drug resistance is a serious problem. Under the selective pressure induced by an antibacterial agent, initially, susceptible populations of bacteria become resistant to that

agent and proliferate and spread. Antibiotic resistance genes can be transferred between bacteria using three different lateral DNA transfer processes:

Transformation, in which bacteria acquire genes through the uptake of (foreign) DNA from their surroundings.

Transduction, in which bacteria obtain genes through viral DNA infection. Because of the high concentrations of viruses (bacteriophages) in aquatic habitats, seawater, and marine sediment, this alternative has the potential to play an important role in resistance transference.

Conjugation, i.e., bacteria gain genes by cell-to-cell mating. In this process, a plasmid is passed from one organism to another through a pilus. This may occur between members of same species or between bacteria from different genera or families. The spread of genes coding for antibiotic resistance is facilitated by mobile genetic elements called transposons, which can move from plasmids to the bacterial chromosome and in the reverse direction. A large family of discrete mobile genetic units called cassettes has been described; these elements act similarly to transposons. Cassettes may contain only one antibiotic resistance gene and a family of receptor elements called integrins that provide both the site into which gene cassettes are integrated and the enzyme responsible for gene movement (integrase). This enzyme can move these resistance cassettes in and out of the integrin, thereby substantially increasing the horizontal mobility of antibiotic resistance genes and allowing bacteria to quickly adapt to environmental changes.

Antibiotic effects on environmental bacteria

The effects of fish farming on bacterial density, biomass, and community structure and the possible connections between these factors and antibiotic resistance have been investigated. Several studies have been conducted; however, the overall results are still debatable. When antibiotic treatment is initiated (usually through the medicated feed), the gut microbiota and environmental bacteria may encounter antibiotics found in fish farms and hatchery waste. Infectious treatment of salmonids with various antibiotics (including OTC oxytetracycline) has been shown to result in significant increases in the proportion of the gut microbiota displaying antibiotic resistance (Austin and Al-Zahrani, 1988).

Oxytetracycline, one of the most commonly used antibiotics in fish farms and hatcheries, is very poorly absorbed by fish. It must be given at a high dose of 100–150 mg per kg of fish per day for 10–15 days. As a result, this treatment causes the slow excretion of large amounts of this antibiotic, increasing selective pressure and potentially leading to the selection of oxytetracycline-resistant bacteria in the gut. The isolates carrying the floR gene showed a high incidence of multi-drug resistance, all strains were resistant to at least five of the following antibacterial drugs: ampicillin, cefotaxime, streptomycin, kanamycin, gentamicin, chloramphenicol, florfenicol, oxytetracycline, nalidixic acid, and oxalinic acid, flumequine, furazolidone and trimethoprim-sulfamethoxazole (Fernández-Alarcón, 2010).

Antibiotics and their effects on fish stress responses

The use of antimicrobial drugs in aquaculture has well-known positive effects on the control of bacterial infections; however, excessive use is associated with several side effects that affect both the fish and the environment. When one considers that 70 to 80% of antibiotics administered to fish in the form of medicated pelleted feed are excreted into the aquatic environment via urinary and faecal excretion and/or as unused medicated food, it is easy to imagine how antibiotics can affect aquatic habitats. Rijkers and colleagues conducted one study that revealed a disparity between different administration routes. They investigated the *in* *vivo* effects of oxytetracycline, either orally in the feed or intraperitoneally, on immune function in carp. Allogeneic-scale transplantation was used to determine the effects on cellular immunity. In the case of oral administration, they discovered that there was no effect on the scales' median survival time (MST). However, the injected fish had a significantly longer MST (11–20 days) than the control fish (8.5 days). (Rijkers *et al.,* 1981) Currently, only a few reports on the effects of oxytetracycline, florfenicol, and, to a lesser extent, oxalinic acid on the fish immune system have been published. Oxytetracycline has been shown to suppress immune functions in carp, rainbow trout, turbot, and Atlantic cod. The first studies were conducted *in vitro* and revealed that oxytetracycline suppressed mitogenic and allogenic leukocyte responses in fish and that low concentrations of this antibiotic delayed but did not reduce the mitogenic response (Grondel *et al.,* 1985).

Antibiotics and public health

The use of antibiotics in aquaculture is governed by local regulations, which vary greatly between countries. Some countries have strict regulations on antibiotic use, and only a few antibiotics are licensed or use in aquaculture. However, a significant portion of global aquaculture production occurs in countries with permissive regulations. Furthermore, many governments have set obligatory Maximum Residue Levels (MRLs) for aquaculture products. The amount of antimicrobial encountered or consumed, *i.e*, the exposure In December 2003, an FAO/OIE/WHO consultation on scientific concerns relating to non-human antimicrobial use was conducted in Geneva. It was established that antibiotic residues in foods provide a substantially lower risk to human health than antimicrobial-resistant microorganisms in foods. Antibiotic-resistant bacteria in animal-derived foods pose a possible health risk because resistance can be passed across bacteria, and antibiotic-resistant diseases may not respond to antibiotic treatments, (Romero *et al.,* 2012). Antimicrobial-resistant bacteria in aquaculture pose a public health risk. The appearance of acquired resistance in fish pathogens and other aquatic bacteria means that such resistant bacteria can serve as a reservoir of resistance genes from which genes can spread further and may eventually end up in human pathogens. Through conjugation, plasmid-borne resistance genes have been transferred from the human-derived bacterium *Escherichia coli*, certain strains of which are harmful to fish, and to humans. In other instances, the human cholera-causing bacterium *Vibrio cholera* has acquired plasmid-borne drug-resistance genes from the fish pathogen *Vibrio anguillarum* (Nakajima *et al*,.1983).

Possible Actions

The natural biodegradation of antibiotics in the environment may not be an adequate option for their eradication. Some of these products, such as quinolones, take several months to degrade. Drug resistance is a multifaceted concern that has little chance of improvement because resistance is not reversible. Therefore, there is an urgent need to embark upon it in a determined manner (Vignesh *et al.,* 2011).

1. Synchronization between human, veterinary, and environmental sectors to recognize the magnitude of the relationships among the occurrences of antimicrobial resistance in humans, animals, and the environment.
2. Enforcement of existing legislation. Approximately 80% of the world's aquaculture production originates in countries with either scarce boundaries on antimicrobial use or negligent enforcement.
3. Forestall the development and extension of antimicrobial resistance by reducing the need for antibiotic treatment is most effective.
4. Imparting education about the sensible use of antibiotics in the aquaculture sector is needed.

5. The most effective means to forestall the development and extend of antimicrobial resistance is to reduce the need for antibiotic treatment.

Policies for antibiotic use in aquaculture

Antibiotic-resistant bacteria and antibiotic-resistance determinants migrate from aquatic to terrestrial environments. Many countries have severely restricted the use of antibiotics in aquaculture due to concerns about the terrestrial environment. Increased control of therapeutic antibiotic prescription, almost total elimination of antibiotic prophylaxis in this setting, and prohibition of the use of antibiotics in therapeutics those are still very useful in the therapy of human infections. This tighter control over antibiotic use, combined with sanitary measures such as vaccine use, has resulted. The use of antibiotics in the aquaculture industry of developed countries has been drastically reduced, indicating that it is economically feasible to develop a productive aquaculture industry without excessive prophylactic antibiotic use. However, in countries with growing aquaculture industries, such as China and Chile, the use of quinolones and many other antibiotics is completely unrestricted (Jacoby, 2005; Cabello, 2004).

Conclusion

Large quantities of antibiotics are used in aquaculture in some countries. China, Indonesia, Egypt, India, Vietnam. They are used not only to treat diseases but also for prophylaxis. Consequently, many problems are associated with the use of antibacterial in aquaculture. More research is needed in order to determine the consequences of the application of large quantities of antibacterial. Considering the rapid growth and importance of the aquaculture industry in many regions of the world and the widespread, intensive, and often unregulated use of antibacterial agents for fish and shellfish production, additional efforts are required to prevent the development and spread of antibacterial resistance in aquaculture.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

Conflict of interest

The authors declare that the manuscript was formulated in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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