Antibiotics in Aquaculture

[Article ID: SIMM0301]

Ulaganathan Arisekar
Ph.D. Research Scholar,
Department of Fish Quality Assurance and Management, Fisheries College and Research Institute, Tamil Nadu Fisheries University, Thoothukudi, Tamil Nadu

Summary

Globally, aquaculture plays a significant role in supplying approximately 8% of the total animal protein intake in the human diet. Furthermore, the per capita consumption of aquaculture products is increasing at a more rapid rate in comparison to meat and dairy consumption. Concerns have arisen regarding the excessive use of antimicrobials within the fast-growing aquaculture sector, which could potentially contribute to the emergence of antimicrobial resistance. This situation poses potential risks to the well-being of animals, humans, and ecosystems alike. However, there exists a notable dearth of comprehensive data on the quantitative utilization of antimicrobials across the diverse aquaculture industry. Antibiotics have been widely and effectively employed in aquaculture, primarily due to the industry's rapid expansion. Nevertheless, this widespread antibiotic use has given rise to substantial health challenges within the aquaculture sector, as well as among other animal populations and even humans. The extensive application of a variety of antibiotics, including non-biodegradable forms, results in their prolonged presence within aquatic ecosystems. As a consequence, this persistence has contributed to the emergence of antibiotic-resistant bacteria within these environments. This, in turn, has led to an increase in antibiotic resistance among fish pathogens, the transmission of these resistance genes to bacteria in terrestrial animals, and the potential to impact human health negatively. Additionally, this practice has disrupted the bacterial communities within both sediment and water columns. Therefore, there is an urgent need for global initiatives to promote the more cautious and regulated use of prophylactic antibiotics in aquaculture.

Introduction

In 1928, Alexander Fleming, a Scottish bacteriologist, made a significant observation while studying bacterial cultures. He noticed that colonies of bacteria on a culture plate had been negatively impacted by the presence of a mold called *Penicillium notatum*, which had accidentally contaminated the culture. Around a decade later, a team of researchers including British biochemist Ernst Chain and Australian pathologist Howard Florey successfully isolated the active compound responsible for this effect and named it penicillin. Their ground-breaking work showcased penicillin's remarkable effectiveness in treating a wide range of severe bacterial infections. As time passed, scientists in the late 1950s began exploring ways to modify the core structure of the penicillin molecule by adding various chemical groups. These efforts resulted in the development of semisynthetic versions of penicillin, significantly expanding the range of antibiotics available for the treatment of diseases caused by various types of bacteria, including staphylococci, streptococci, pneumococci, gonococci, and the spirochaetes responsible for syphilis. Antibiotics, hailed as one of humanity's most significant discoveries, have played a crucial role in controlling bacterial infections for over 85 years. They have been employed in human medicine, animal husbandry, and agriculture. Unfortunately, their use has surged in the food-animal production sector due to their growth-promoting properties. This indiscriminate use of antibiotics in both developed and developing countries has led to several concerning issues. The overuse and misuse of antibiotics have resulted in the development of resistance in pathogenic and environmental microbes. Additionally, the accumulation of antibiotic residues in the environment has caused toxicity concerns. This situation also threatens the natural populations of microfauna, which play a pivotal role in maintaining environmental balance. Given the indispensable role of antibiotics in healthcare and food production, their responsible use is paramount. It's worth noting that bacteria can develop resistance to antibiotics at a faster rate than new antibiotics are being developed. Unfortunately, there has been no introduction of a new class of antibiotics in the past four decades. Therefore, preserving the effectiveness of existing antibiotics is of utmost importance for human health and sustainable food production. Furthermore, there is growing concern about the presence of pharmaceutically active chemicals in the aquatic environment, posing a significant health risk. The widespread use of antibiotics in healthcare facilities, livestock, poultry, and aquaculture farms, coupled with the improper disposal of waste and wastewater from municipalities, animal farms, and the pharmaceutical industry into bodies of water like rivers and lakes, has exacerbated the issue of antibiotic resistance. In addition to these concerns, the consumption of animal protein has surged in Asia, with per capita consumption rising from seven to twenty-five grams over five decades. This increased demand for animal products further underscores the importance of responsible antibiotic use in agriculture to ensure both human health and environmental sustainability

WHAT ARE ANTIBIOTICS

Antibiotics have emerged as a pivotal discovery within the last 85 years, revolutionizing the management of bacterial infections across diverse domains such as human healthcare, animal husbandry, fisheries, and agriculture. These invaluable compounds encompass a spectrum of natural, semi-synthetic, and synthetic substances, all endowed with potent antimicrobial properties and amenable to various modes of administration, including oral, parenteral, and topical routes. Within the realms of both human and veterinary medicine, antibiotics assume a multifaceted role, serving as agents to combat bacterial, fungal, and protozoan ailments while also stimulating growth in livestock. In accordance with the World Health Organization's classification, antibiotics represent synthetic or semi-synthetic compounds employed as medicinal remedies to both forestall and alleviate bacterial and fungal infections (WHO, 2019). Furthermore, it is important to note the presence of residual traces, comprising minute quantities of utilized antibiotics or their metabolites, which may persist within the flesh of aquatic organisms (USFDA, 1989 & EC, 2009).

CONSUMPTION OF ANTIMICROBIAL TRENDS IN FOOD ANIMALS

Since 2001, global aquaculture has consistently grown at an annual rate of 5.8%, driven by the increasing demand for animal protein in developing economies. Currently, aquaculture provides nearly half of the world's seafood for human consumption, with Asia leading the industry, responsible for almost 90% of global production. In 2016, China alone accounted for 61% of worldwide aquaculture output, representing a third of all fish products consumed by humans. This growth in animal-based nutrition has led to more intensive production methods, including the non-therapeutic use of antimicrobials to stimulate growth and compensate for suboptimal practices. The excessive use of antimicrobials in both humans and food-producing animals is a major driver of antimicrobial resistance, a critical global health challenge. In aquaculture, intensification and the rise of aquatic animal pathogens have further increased antimicrobial use and resistance. Global antimicrobial use in animal food production was 63,151 tons in 2010 and is projected to increase by 67% to 105,596 tons by 2030, primarily due to the growing number of animals raised for food. Asia is expected to witness a 46% increase in antimicrobial consumption by 2030, reaching 51,851 tons, making up 82% of the global consumption in 2010. In 2010, China, the United States, Brazil, Germany, and India were the top consumers of antimicrobials in food animal production. By 2030, Myanmar, Indonesia, Nigeria, Peru, and Vietnam are expected to experience the highest percentage increases in consumption. Notably, the use of antimicrobials in aquaculture can lead to their release into aquatic ecosystems, affecting ecosystem health, biodiversity, and freshwater availability. Aquaculture operations may also act as reservoirs for antimicrobial resistance genes, potentially transmitting them to humans and other animals

Common Antibiotic Families and their Mechanisms of Action:

1. Beta-lactams: Block bacterial cell wall synthesis (e.g., Penicillins, Cephalosporins, Carbapenems).
2. Macrolides: Halt bacterial protein synthesis (e.g., Erythromycin, Azithromycin, Clarithromycin).
3. Tetracyclines: Interfere with bacterial protein synthesis (e.g., Tetracycline, Doxycycline, Minocycline).
4. Aminoglycosides: Inhibit bacterial protein synthesis (e.g., Gentamicin, Tobramycin, Amikacin).
5. Fluoroquinolones: Disrupt bacterial DNA synthesis (e.g., Ciprofloxacin, Levofloxacin, Moxifloxacin).
6. Sulfonamides: Impede bacterial folate synthesis (e.g., Trimethoprim-sulfamethoxazole, TMP-SMX).
7. Glycopeptides: Hinder bacterial cell wall formation (e.g., Vancomycin, Teicoplanin).
8. Oxazolidinones: Interrupt bacterial protein synthesis (e.g., Linezolid).
9. Streptogramins: Includes quinupristin and dalfopristin.
10. Polymyxins: Includes colistin and polymyxin B.
11. Nitrofurans: Includes nitrofurantoin and furazolidone.
12. Fusidane-type Antibiotics: Exemplified by fusidic acid and helvolic acid.

ANTIBIOTICS IN AQUACULTURE

The global human population has been steadily increasing, leading to a surge in consumption, particularly concerning animal protein. Consequently, there is an unprecedented rise in the demand for animal protein worldwide. To address this protein demand, intensive aquaculture farming has emerged as a viable solution. Much like traditional livestock farming, aquaculture farming, which encompasses fish, crustaceans, mollusks, and more, has gained prominence as a significant contributor to global protein production. At present, over 580 different aquaculture species are being cultivated on a global scale. However, it's essential to highlight that the current practice of aquaculture farming is closely associated with the widespread use of antimicrobial agents. Antimicrobial drugs play a pivotal role in managing infectious diseases in food animals and aquaculture. They are commonly employed for purposes such as animal therapy, disease prevention, and as growth promoters. Regrettably, the imprudent utilization of antimicrobials in both food animals and aquaculture has become a key driver in the escalating problem of antimicrobial resistance. Across the globe, more than a hundred different antimicrobial agents, including but not limited to β-lactams, aminoglycosides, tetracyclines, phenicols, macrolides, sulfonamides, fluoroquinolones, lincosamides, and polypeptides, have been harnessed for the production of aquaculture-related food products. It's important to recognize that there are justified applications of antibiotics in specific situations. Antibiotics are primarily utilized to combat or eradicate rapidly invading microorganisms that can potentially harm the animals and impede their growth. They may be administered as a preventive measure or as a treatment for infections. The mechanism through which antibiotics act as growth promoters is closely tied to their interaction with the gut microbiota, as elucidated by Ni et al. in 2021. Nevertheless, it's crucial to monitor antibiotic usage carefully, as residues of these drugs can persist in trace amounts within the edible portions of animal products after administration. Exceeding acceptable maximum residue limits of antibiotics in food animals may contribute to the development of antibiotic resistance in both animals and humans. Therefore, antibiotics are employed in aquaculture not only for growth promotion but also to control bacterial, fungal, and viral diseases.

Therapeutic:
Treatment - Individual or few sick animals treated with antibiotic. *e.g.* Chloramphenicol, ciprofloxacin, tetracyclines

Prophylactic:
Prevention – sick and healthy animals treated with antibiotics. *e.g.* Tetracyclines, Erythromycin, AOZ, and Malachite green

Growth promotor:
Specific for growth of animals - Very low sub-therapeutic doses. *e.g.* Tetracyclines, AOZ, enrofloxacin

Table 1. List of antibiotics approved for aquaculture uses as per the USFDA

Approved Drugs	Dosage/time	Diseases
Chloramine (Antimicrobial)	20ppm/40 m	Furunculosis, Gafkemia, columnaries, Enteric Red mouth,
Formalin (Parasiticide)	25ppb/1hr	Parasitic infection
Tetracycline hydrochloride (Antimicrobial)	500 ppm/4hr	Furunculosis, Gafkemia, Hemorrhagic septicemia, columnaries Enteric Red mouth
Florfenicol (Antimicrobial)	10 ppm/30m	Furunculosis
Hydrogen Peroxide (Fungicide)	500-700 ppm/15 m	Common fungal infection (dipping treatment)
Oxytetracycline (Antimicrobial)	1g/Ib/15m	Furunculosis, Gafkemia, Hemorrhagic septicemia, Enteric red mouth,
Ormetoprim (Antimicrobial)	50 ppm/30m	Furunculosis, Enteric red mouth, Vibriosis, luminescent diseases
Sulfamerazine (Parasiticide/antimicrobial)	NA	Furunculosis, Enteric red mouth, Vibriosis
Tricaine methanesulfonate (parasiticide/anaesthetic)	1000ppm/10m	NA

Source: USFDA, 2021

Table 3. List of antibiotics and other pharmacologically active substances banned for use in shrimp aquaculture

Sl.	Antibiotics and other Pharmacologically Active substances
1.	Chloramphenicol
2.	Nitrofurans including: Furaltadone, Furazolidone, Furylfuramide, Nifuratel, Nifuroxime, Nifurprazine, Nitrofurantoin, Nitrofurazone
3.	Neomycin
4.	Nalidixic acid
5.	Sulphamethoxazole
6.	Aristolochia spp and preparations thereof
7.	Chloroform
8.	Chlorpromazine
9.	Colchicine
10.	Dapsone

11.	Dimetridazole
12.	Metronidazole
13.	Ronidazole
14.	Ipronidazole
15.	Other nitroimidazoles
16.	Clenbuterol
17.	Diethylstilbestrol (DES)
18.	Sulfonamide drugs (except approved Sulfadimethoxine, Sulfabromomethazine and Sulfaethoxypyridazine)
19.	Fluroquinolones
20.	Glycopeptides

Source: CAA, 2021

Regulatory Authorities/Schemes in India

- ✓ The Central Drugs Standard Control Organization (Approval and Banned, New Delhi)
- ✓ Food and Drug Administration (FDA, Mumbai)
- ✓ MPEDA - National Residue Control Plan (NRCP)- (EU monitoring)
- ✓ MPEDA- Pre-Harvest Testing (Notified)
- ✓ Export Inspection Council (Notified)
- ✓ Coastal Aquaculture Authority (Approved)

Conclusion

To summarize, collectively underscore the widespread use of antibiotics in shrimp farming practices. These antibiotics are often employed prophylactically and administered daily, leading to the utilization of numerous antibiotic types. Unfortunately, many farmers lack adequate knowledge regarding safe and efficient application practices. The overuse of antibiotics not only contributes to the development of antibiotic resistance in both aquatic pathogens and humans but also facilitates the transfer of resistance genes among aquatic bacteria, potentially affecting human pathogens. Given the rapid growth and global significance of the aquaculture industry and the often-unregulated use of antimicrobial agents within it, the need for proactive measures to prevent antimicrobial resistance in aquaculture is paramount. These measures should include improved management practices, regulatory controls on antibiotic usage, prudent use guidelines, and ongoing monitoring of antibiotic use and resistance development. Disseminating information plays a pivotal role in achieving these goals without compromising shrimp production levels.

REFERENCES

CAA, 2021. List of Antibiotics and other pharmacologically active substances banned for using in shrimp aquaculture.Coastal Aquaculture Authority, Govt. of India, Chennai. http://caa.gov.in/uploaded/doc/Pharmacologically.pdf

Ibrahim, M., Ahmad, F., Yaqub, B., Ramzan, A., Imran, A., Afzaal, M., Mirza, S.A., Mazhar, I., Younus, M., Akram, Q., Taseer, M.S.A., 2020. Current trends of antimicrobials used in food animals and aquaculture. In Antibiotics and antimicrobial resistance genes in the environment. Book chapter Elsevier, 39-69

MPEDA, 2020. Handbook of Fisheries Statistics. Marine product Export Development Authority, Govt. of India, Cochin. https://mpeda.gov.in/wp-content/uploads/2021/06/Handbook-of-Fisheries-statistics-2020.pdf.

MPEDA, 2021. State wise aquaculture production. Marine product Export Development Authority, Govt. of India, Cochin. https://mpeda.gov.in/?page_id=651.

Ni, L., Chen, D., Fu, H., Xie, Q., Lu, Y., Wang, X., Zhao, Y., Chen, L., 2021. Residual levels of antimicrobial agents and heavy metals in 41 species of commonly consumed aquatic products in Shanghai, China, and cumulative exposure risk to children and teenagers. Food Control, 129, 108225.