Sri Lanka J. Aquat. Sci. ***23(1)*** *(2018): 13-27* http://doi.org/10.4038/sljas.v23i1.7543

Heavy use of antibiotics in aquaculture: Emerging human and animal health problems – A review

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Abstract Antibiotics have been extensively and effectively used in aquaculture due to accelerated growth of aquaculture and this has resulted in the development of serious health problems in aquaculture, other animals, and human. The use of a wide variety of antibiotics in large amounts, including non-biodegradable antibiotics, ensures that they remain in the aquatic environment for a long time. This has resulted; the emergence of antibiotic-resistant bacteria in the environments, an increase of antibiotic resistance in fish pathogens, transfer of these resistance determinants to bacteria and then land animals and finally become human pathogens along with alterations of the bacterial flora both in sediments and in the water column. Thus, the global efforts are needed to promote more judicious use of prophylactic antibiotics in aquaculture as accumulating evidence indicates that unrestricted use is detrimental to fish, terrestrial animals and human health.

Keywords: aquaculture, antibiotics resistance, environmental contamination, human health, risk management

INTRODUCTION

The aquaculture has rapidly grown in the worldwide as a major industry, providing not only economic income and high-quality food product, but also provides employment to hundreds of thousand skilled and unskilled workers. It has been predicted by 2050, the total population of the planet will be around 9 billion. Therefore, aquaculture will have an important role in catering to the increased demand for protein food (Godfray et al. 2010). It has been identified that all animal production system has challenges associated with disease and the best way to solve this is often through effective management practices via management of stock, soil, water, nutrition, and environment (Ringo et al. 2014). Further, it has been identified that problems related to diseases and deterioration of environmental quality parameters often occurs and the final result may end up with serious economic losses (Balcazar et al. 2006). Hence, diseases in aquaculture systems are now considered as one of the critical limiting factors in this industry and special emphasis was given to shrimp aquaculture (Purivirojkul and Khidprasert 2009).

Many scientific studies have revealed that infectious diseases have remained as a significant problem in aquaculture system worldwide, and proper management approaches should be taken to mitigate against the effect of pathogens in farmed animals. Therefore, the methods of controlling diseases in aquaculture with management practices are given in Table 1 (Newaj-Fyzul et al. 2014). Recent studies to date have shown that several antimicrobial drugs including antibiotics have been approved and used in many countries to treat bacterial diseases in aquaculture and number of antibiotics are being used in aquaculture systems have exerted a very strong selection pressure towards resistance bacteria (Ringø et al. 2014).

The World Organization for Animal Health (WOAH) has developed standards in the Aquatic Animal Health Code (AAHC) on the responsible and prudent use of antimicrobial agents in aquatic animals. A list of Antimicrobials of Veterinary Importance has been published (World Organization for Animal Health 2015), which aims to optimize the balance between animal health needs and public health considerations. To date, there is no harmonized system of surveillance is used worldwide and circulation of antimicrobial agents in aquaculture is widely available. In the world, antibacterial chemicals are being used in aquaculture to prevent and treat bacterial infections in fish and invertebrates (Cabello 2006; Cabello et al. 2013). For examples, in the United Kingdom sale of 2 tonnes of antibiotics are used in the production of fish (UK-VARSS 2014) where Canada and Norway permit use of oxy-tetracycline, florfenicol and quinolones for aquaculture (Cabello et al. 2013). The classic example is a usage of antibiotic quantity for Salmon cultivation can vary as much as 175-fold (e.g., 0.008–1.4 kg of antimicrobial) which is depended on country of the production (Cabello et al. 2013). The most abundant antibiotic quinolone (by mass) used in Norway for Salmon production was 821,997 tonnes in 2007), followed by oxolinic acid (681 kg in 2008), florfenicol, a synthetic derivative of chloramphenicol (166 kg in 2010) and oxytetracycline (23 kg in 2012) respectively (Burridge et al. 2010). Commonly used antibiotic classes in aquaculture sector, route of administration and their structures are given in Table 2.

Table 1. Methods of management practices of control diseases in aquaculture system in the world (Newaj-Fyzul et al. 2014)

Method	Management practices with comments
Animal husbandry/ Management	Improved hygiene including sanitary disposal of dead animals; do not overstock and overfeed
Movement restrictions	Effective at preventing the spread of diseases; essential to have governmental support
Dietary supplements	Effective with compounds such as vitamin C
Vaccine	Available commercially for a minority of diseases
Probiotics	A wide range of probiotics has been considered for use in aquaculture
Prebiotics	Compounds that support the growth of probiotics; of increasing interest to aquaculture
Biological control	The application of inhibitory microorganisms often to water; may be effective but some concerns over the fate of the inhibitors
Antimicrobial compounds	There are emotive issues in many countries about the non-medical use of medicinal compounds

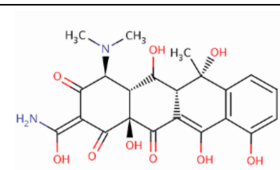
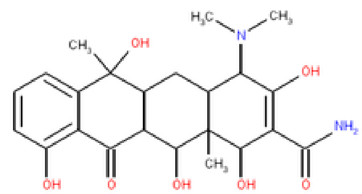
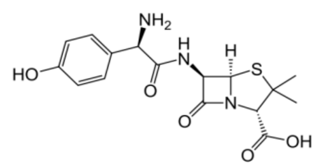
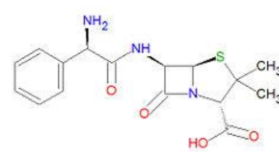
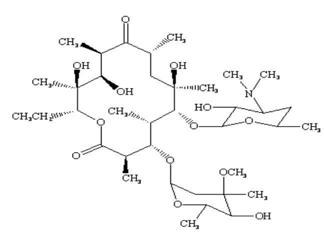
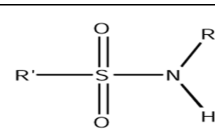
ANTIBIOTIC USAGE IN SOUTH ASIAN COUNTRIES

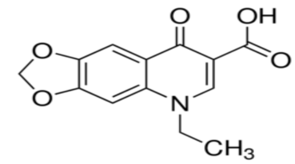
Aquaculture already produces nearly half of the world's food fish and South Asia is the main countries which contribute more than 70% of the production of food fish (Bakar et al. 2013). Some South Asian Countries namely Vietnam, Thailand, Indonesia in the region has considerably developed their aquaculture sectors over recent decades, partly for the export market (Impens et al. 2003). Thus, the area is considered to be a hotspot of Antimicrobial Resistance (AMR). This represents a further risk of dissemination of AMR organisms and genes to consumers worldwide.

According to reported data, the use of antibiotics in aquaculture contributes equally to residues in the environment. Studies from Bangladesh, India, Indonesia, and Thailand have reported antibiotic residues in aquaculture products and aquaculture water (Impens et al. 2003; Bakar et al. 2013). Chloramphenicol was recorded in fish from Bangladesh (~5ng/L) (Bakar et al. 2013) and in shrimps from India (~32ng/L) (Baker et al. 2013) and Indonesia (~45ng/L) (Impens et al. 2003). In Thailand, erythromycin and tetracyclines were detected in aquaculture water up to 180 ng/L (Shimizu et al. 2013), whereas fluoroquinolones were detected in higher concentration (avg. 5130 ng/L, max 46100 ng/L) than aquaculture wastewater in Vietnam (avg. 235, max 1130 ng/L) (Pham et al. 2015). In India, average peak water concentrations in aquaculture farms for Oxytetracycline (OTC) and Erythromycin were recorded as 49 µg/L and 1.6 µg/L (Koeypudsa et al. 2010) respectively while OTC were frequently detected in sediments with concentrations up to 6908 µg/kg (Koeypudsa et al. 2010).

When considered the Sri Lankan situation, despite the long history of antibiotic usage, information regarding antibiotic production and usage patterns are severely limited due to the lack of coordinated and comprehensive monitoring and documenting efforts. Thus, this review paper aims to discuss environmental contamination status of some selected antibiotics in aquaculture farm effluents in Sri Lanka as well.

Table 2. Commonly used antibiotic classes in Aquaculture (Source: WHO 2005)

Antibiotic agent (class)	Route of administration in aquaculture	Structure
Oxytetracycline (tetracyclines)	Oral/bath/injection	
Tetracycline (tetracyclines)	Oral/bath/injection	
Amoxicillin (aminopenicillins)	Oral	
Ampicillin (aminopenicillins)	Oral	
Erythromycin (macrolides)	Oral/bath/injection	
Sulphonamides (sulphonamides)	Oral	

Oxolinic acid (Quinolones)	Oral	

MAJOR PATHWAYS OF ENVIRONMENTAL CONTAMINATION OF ANTIBIOTICS

Hygienic shortcomings in fish raising methods, including increased fish population densities, crowding of farming sites in coastal waters, lack of sanitary barriers and failure to isolate fish farming units with infected animals (Naylor and Burke 2005), have increased the possibility of the rapid spread of microbial infections in aquaculture.

Antibiotic Resistance

This scenario results in an augmented use of prophylactic antibiotics, often with the misplaced goal of forestalling these sanitary shortcomings (Grave et al. 1999; Sørum 2006) because, fish are given antibiotics as a component of their food, and occasionally in baths and injections (Sørum 2006; Gao et al. 2012). However, antibiotics can be metabolized after administration; but up to 80% of antibiotics administrated are excreted in urine or feces without complete decomposition (Muziasari et al. 2014). Therefore, it is possible that antibiotics can find their way into the aquatic environment from a variety of sources such as the excretion of animals and discharge from sewage waste treatment plants. Also, the unconsumed food and fish faeces containing antibiotics reach the sediment at the bottom of the raising pens; antibiotics are leached from the food and faeces and diffuse into the sediment and ultimately they can be washed away by currents to distant sites were recorded (Kerry et al. 1996; Hoa et al. 2011). Thus, the prophylactic and therapeutic use of antibiotics results in the occurrence of Antibiotic-Resistant Bacteria (ARB) and Antibiotic Resistance Genes (ARGs) in the aquaculture environment (Ritter et al. 2008).

The most important issue of antibiotic release into the environment is the development of antibiotic resistance which has resulted in the reduction of therapeutic potential against human and animal pathogens (SCAN 2003; Liyanage and Manage 2016 a). Inappropriate and irrational use of antimicrobial agents provides favorable conditions for resistant microorganisms to emerge, spread and persist (Diwan et al. 2010). The greater the duration of exposure of the antibiotic has the greater the risk of the development of resistance, irrespective of the severity of the need for the antibiotic. Antibiotic resistance towards particular antibiotics becomes more common and a greater need for alternative treatments has arisen (Bush et al. 2011). Antibiotic resistance will develop in five different mechanisms was identified and explained so far as; alterations of the target site of the antibiotic, enzymatic inactivation of antibiotics, reduction of the inner and outer membrane permeability, flush out of the drug and using an alternative metabolic pathway.

MECHANISMS OF RESISTANCE TO ANTIBIOTICS

Alteration of target site of the antibiotic (Mechanism 1)

Connections of the antibiotic target areas are different. They can be various enzymes and ribosomes. Resistance associated with the alterations in the ribosomal target is the most frequently observed in macrolide antibiotics. Also, this is common for developing resistance to beta-lactams, quinolones, and tetracycline (Paterson et al. 2005; Bush et al. 2013).

Enzymatic inactivation of antibiotics (Mechanism 2)

Most of the gram positive and gram negative bacteria are synthesized enzymes that degrade antibiotics. In this group, beta-lactamases, aminoglycosides, modifying enzymes (acetylase, fosforiaz adenilaz) are potentially degraded beta-lactam antibiotics and continually increasing their number of which inactivates enzymes include chloramphenicol and erythromycin (Paterson et al. 2005; Bush et al. 2013).

***Reduction of the inner and outer membrane permeability* (Mechanism 3)**

This resistance decrease in drug uptake into the cell or quickly ejected from the active resistance of the pump systems. Reduction in permeability of the outer membrane may play an important role in resistance to quinolones and aminoglycosides (Thomas and Nielsen 2005).

***Flush out of the drug (efflux pump)* (Active *Pump System)* (Mechanism 4)**

The production of complex bacterial machinery capable to extrude a toxic compound out of the cell can also result in antimicrobial resistance. Many classes of efflux pumps have been characterized in both gram-negative and gram-positive pathogens. This mechanism of resistance affects a wide range of antimicrobial classes including protein synthesis inhibitors, fluoroquinolones, β-lactams, carbapenems and polymyxins (McMurry et al. 1980)

***Using an alternative metabolic pathway* (Mechanism 5)**

Unlike some of the changes in the target bacteria, a new pathway for drug-susceptible eliminates the need to develop objective. In this way, resistance is seen among the sulfonamide and trimethoprim. Bacteria can gain property of getting ready folate from the environment instead of synthesizing folate (Jacoby et al. 2009). The discussed mechanisms are summarized in Figure 2.

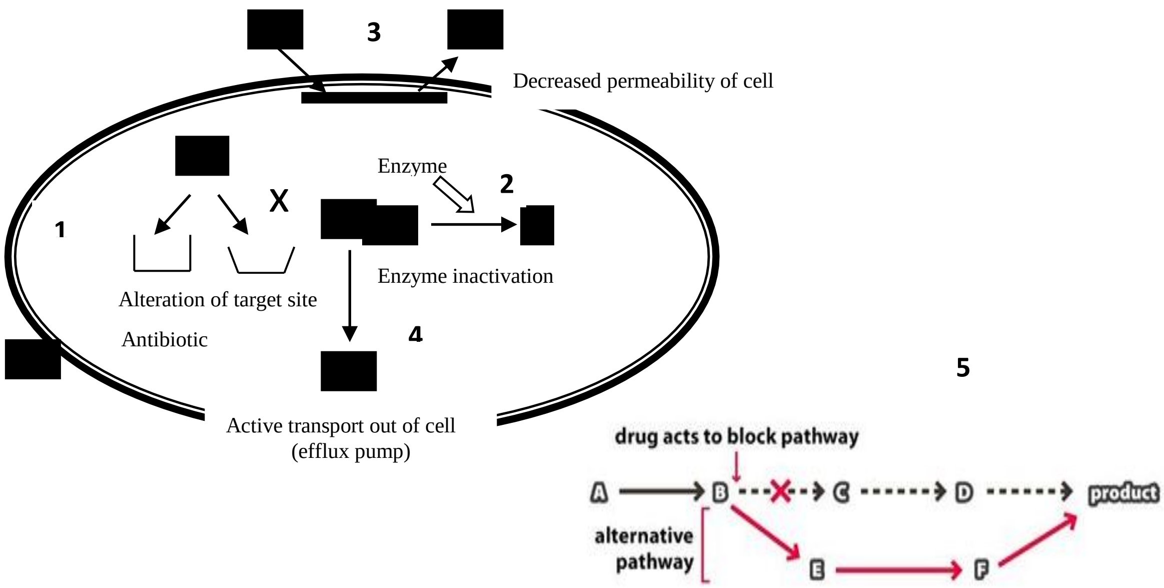


Figure 2. Antibiotic resistance mechanisms (1-alteration of target site; 2-enzyme inactivation; 3-reduction of inner and outer membrane permeability; 4- efflux pump; 5- Using an alternative metabolic pathway)

Transfer of Resistance Genes

When a bacterial cell divides, the chromosome of the bacterium is passed into its daughter cells (Vertical Transfer). But apart from this **Vertical Transfer (VT)**, genetic information can also be passed between bacteria through processes known as **Horizontal Gene Transfer** (HGT). The three main processes of HGT are transformation, transduction, and conjugation. The nature of the genetic elements transferred is an important aspect of HGT. Major processes are; (a) transformation, the uptake of naked DNA via the cell wall, (b) transduction, viral-mediated (phage) gene transfer

(c) conjugation, plasmid transfer from one bacterium to another and the incorporation of that DNA into the existing genome or plasmids (Lewin 1992).

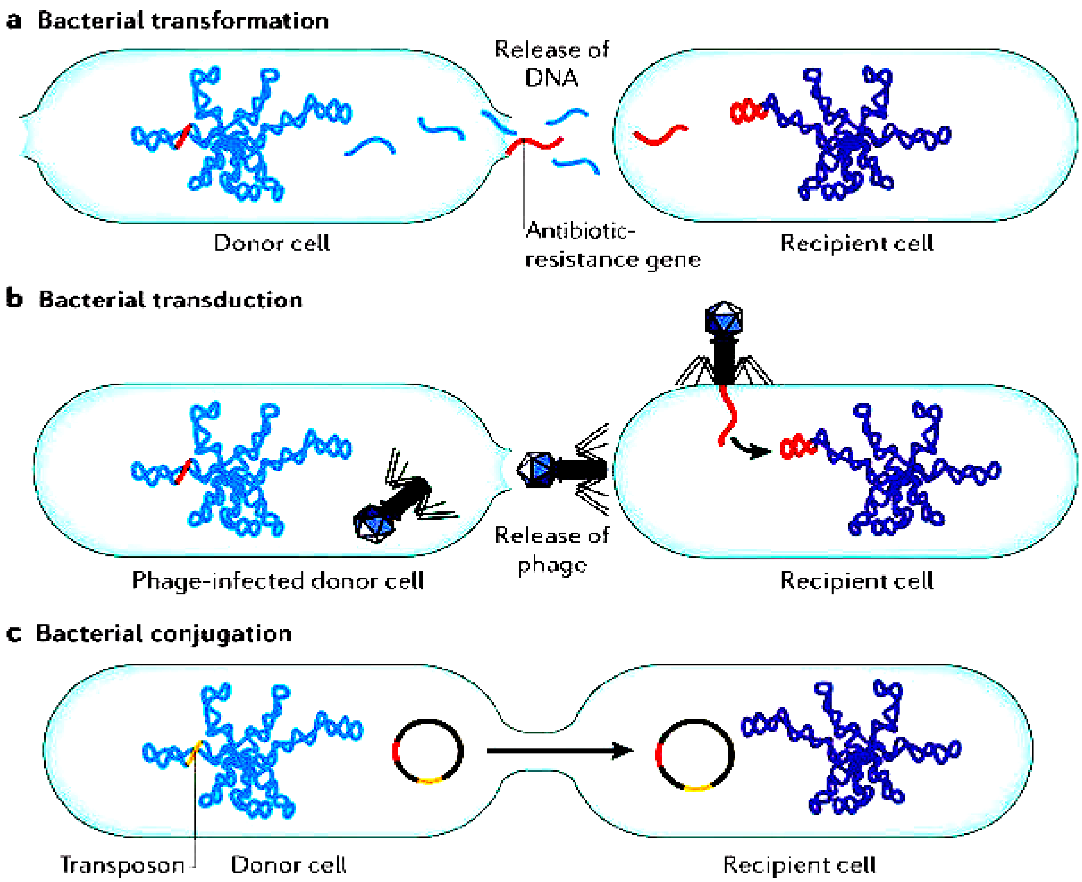


Figure 2. Major pathways in Horizontal Gene Transfer (HGT) (a- Bacterial transformation; b- Bacterial transduction; C- Bacterial conjugation) (Source: Nature Reviews - Microbiology 2006)

It is well documented that fish pathogens and other aquatic bacteria such as *A. salmonicida, A. hydrophila, C. freundii, V. salmonicida, F. psychrophilum* and *P. fluorescens* have developed resistance as a consequence of exposure to antibacterial agents (Sorum 2006). Acquired sulfonamide resistance in *A. salmonicida*, which cause disease in fish that inhibit temperature and cold climates, was reported in 1955 in the United States, and 1960s, multidrug-resistant bacteria strains were recorded in Japan (Suzuki et al. 2008). Since that time, the multidrug resistance of *A. salmonicida* has been described from many countries in various parts of the world, and transferable resistance plasmids were commonly recorded in these strains (Vincent et al. 2015).

Plasmids that carry multidrug-resistant determinants have been shown to be transferable to *E.coli* from *A.salmonicida, A.hydrophila, V.cholerae, Shigella* species, *Salmonella* species and *E.coli* (Suzuki et al. 2008; Sorum 2006). Genes coding for tetracycline resistance in fish farm bacteria and human clinical isolates in Japan has shown high similarity, suggesting that they were derived from the same source (Novais et al. 2012; Vincent et al. 2015). Furthermore, in laboratory experiments, transfer of tetracycline resistance from marine strains of *Photobacterium* species, *Vibrio* species, *Aeromonas* species and *Pseudomonas* species into *E.coli* by conjugation was recorded suggesting that transfer of resistance gene from marine bacteria to bacteria associated with the human gut is possible. Ultimately, resistance genes in the aquatic environment may reach human pathogens and thereby add to the burden of antibiotic resistance in human medicine.

DIRECT SPREAD OF ANTIBIOTIC RESISTANCE

Aquatic environments can be a source of drug-resistant bacteria that can be directly transmitted and cause infections in humans (Pham et al. 2015; Liyanage and Manage 2015). The spread to humans can happen through direct contact with water or aquatic organisms, through drinking water, through handling or consumption of aquaculture products (Suzuki et al. 2008). Direct spread from aquatic environments to humans can be involved human pathogens, such as *V. cholera, V. vulnificus, Shigella* species and *Salmonella* species or opportunistic pathogens, such as *A. hydrophila, P. shigelloides, E. tarda* and *E. coli* (Novais et al. 2012; Vincent et al. 2015). Thus, the occurrence of antimicrobial-resistant *Salmonella* species in aquatic environments is most likely attributable to contamination from human, animal or agriculture environments.

AQUACULTURE IN SRI LANKA

Sri Lanka does not have a tradition of aquaculture, despite the large freshwater and brackish water resources available in the country, there was virtually no aquaculture carried until the beginning of 1980 (Heenatigala and Fernando 2016). Since that time fish culture in seasonal village tanks, marine shrimp culture in coastal earthen ponds and live ornamental fish exports have reached commercial dimensions while other attempted methods such as fish culture in brackish water ponds, cage culture, mollusk and seaweed culture are yet to be developed (NAQDA 2015). At present, in many Asian countries including Sri Lanka, fish is the major protein diet of the local people (82%) because of the consumption habit, health and its nutritional benefits (MFARD 2016). Annual aquaculture production in Sri Lanka has increased from 44300 Mt and 334 890 Mt since 1999 to 2014 (NAQDA 2015). In the shrimp culture industry in Sri Lanka, financial losses due to the infectious diseases have become a major limiting factor in its development (Heenatigala and Fernando 2016). A major concern has been given to the viral infections of shrimps and as a result, their bacterial diseases have received less attention. *Vibrio* spp. are a part of the natural microflora of wild and cultured shrimps (Sinderman 1990) and the members of the family Vibrionaceae contribute to 60% of their total bacteria population (Simidu and Tsukamoto 1985). *Vibrio* bacteria are one of the main pathogenic organisms which cause high mortality in shrimp farming industry. The multitude of infections caused by bacteria belonging to the genus *Vibrio* is referred as vibriosis.

According to WHO, only 14 medicinal products including 7 antibiotic medicinal products (amoxicillin, florfenicol, flumequine, oxolinic acid, oxytetracycline [OXY], sarafloxacin [SARA], and sulfadiazine/trimethoprim) were authorized and approved for aquaculture (WHO 2014). Fluoroquinolones (FQ) and tetracyclines (TC), have also been approved as some additional antibiotics even they are being employed in human therapy (Cabello 2006; Heuer et al. 2009), are also widely used and effective veterinary antibiotics to prevent and treat fish diseases (FAO 2010). However, little information about the contamination status of antibiotics and ARGs are available in Sri Lanka. Therefore, monitoring studies of the antibiotics, ARB and ARGs in Sri Lanka aquaculture industry is necessary to develop safety and profitable aquaculture industry.

Present status of antibiotic contaminations in aquaculture effluent water in Sri Lanka

Effluent in aquaculture sites showed higher concentrations of antibiotics are belonging to tetracycline group compared to the other selected antibiotics tested (Figure 3). TET and OTC were detected at all sites except Dambulla, Muthupanthiya and Udappuwa, where detected OTC levels in shrimp hatcheries (0.056 ± 0.001 µg/ml - 0.234 ± 0.014 µg/ml) were comparably higher than OTC levels in food fish farms (0.008 ± 0.012 µg/ml - 0.221 ± 0.012 µg/ml) and ornamental fish farms (0.009 ± 0.011 µg/ml - 0.031 ± 0.005 µg/ml) (Liyanage and Manage 2016b). Similarly, high TET levels were detected in shrimp hatcheries (0.012 ± 0.019 µg/ml - 0.112 ± 0.017 µg/ml) compared to ornamental (0.001± 0.002 µg/ml - 0.002 ± 0.031 µg/ml) and food fish farms (0.001 ± 0.031 µg/ml - 0.076 ± 0.022 µg/ml) respectively. The measured ERM concentrations in effluents of few aquaculture sites were in low level (~0.001 µg/ml) and antibiotics group such as penicillin and sulfonamide were not detected in effluent samples (Liyanage and Manage 2016b).

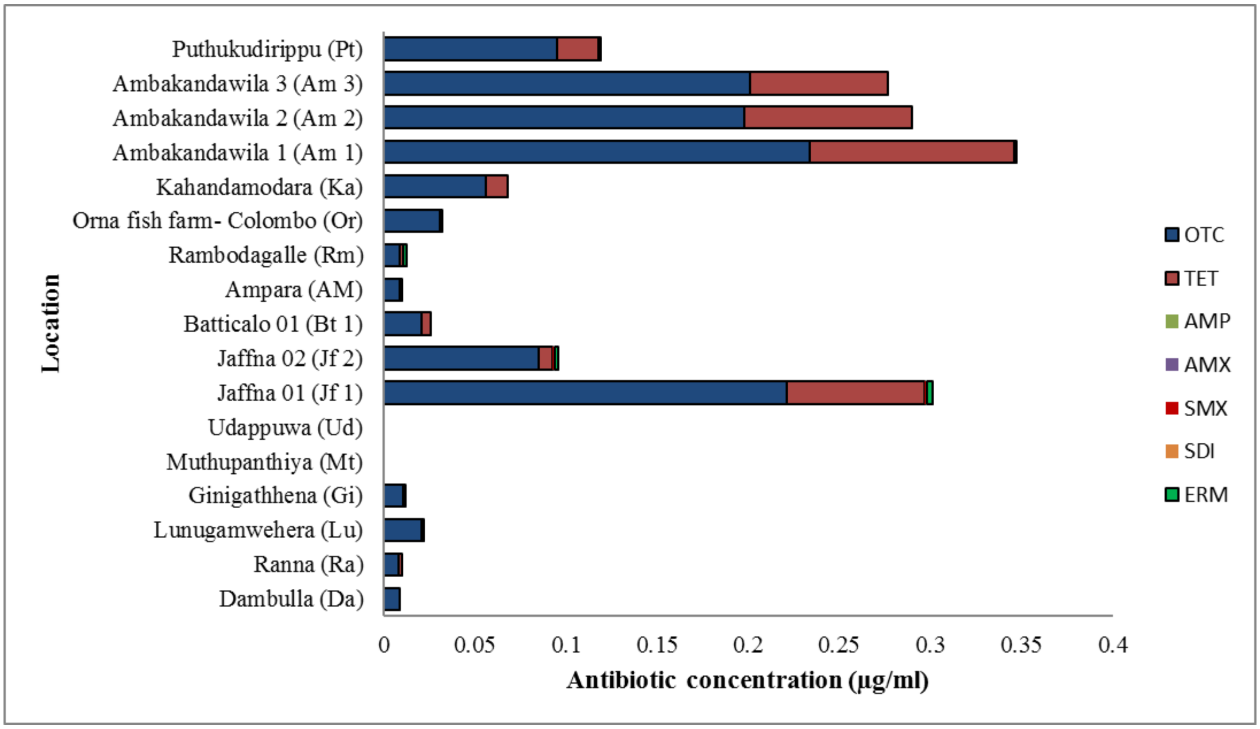


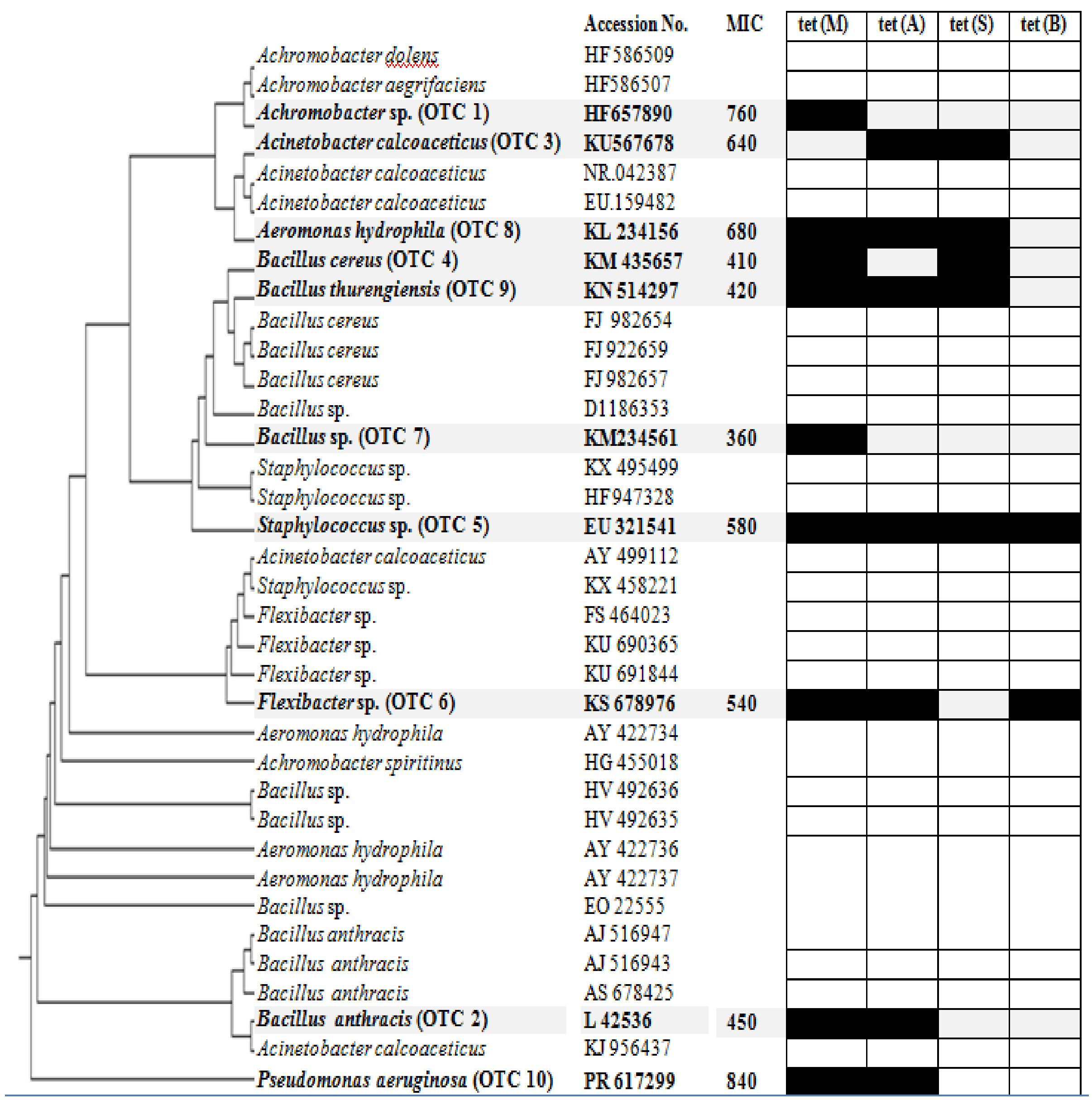
Figure 3. Antibiotic contaminations in aquaculture effluent water in Sri Lanka with studied aquaculture sites (OTC-Oxytetracycline; TET- Tetracycline; AMP- Ampicillin; AMX- Amoxicillin; SMX- Sulfamethoxazole; SDI- Sulfadiazine; ERM- Erythromycin)

In Sri Lanka, *Bacillus* sp., *Acinetobacter* sp., *Achromabacter* sp., *Staphylococcus* sp., *Micrococcus* sp. were identified as most abundant resistance genera for tetracycline and Oxytetracycline in aquaculture farms (Liyanage and Manage 2016b). The isolated strains except *B. thurengiensis* were recorded as pathogenic bacteria which causes different diseases such as fin rot, mouth rot, skin ulcers and abdominal swelling in fish and shrimp (Vincent et al. 2015). MIC values of OTCr bacteria ranged from 360 to 840 µg/ml and the highest was recorded for *Pseudomonas aeriginosa* whereas the lowest was for *Bacillus* sp. MIC values of TETr bacteria were varied from 320 µg/ml to 780 ppm whereas the highest MIC was recorded for the *S. haemolyticus* and the lowest was for the *B. pumilus* respectively (Liyanage and Manage 2016b). The *tet* (M) and *tet* (S) are well studied ribosomal protection protein gene, which is known to distribute widely in the aquatic environment, where *tet*(A) and *tet*(B) are considered as genes efflux tetracycline from the cell. According to figure 4, 11 strains out of 16 isolates were positive for *tet* (M) and *tet* (A), suggesting that these genes were reserved in bacteria which were isolated from wastewater in aquaculture farms. In contrast, *tet* (S) (5/16) and *tet* (B) (4/16) were detected only a few TETr and OTCr isolates respectively (Liyanage et al. 2017).

The industrial development has been accompanied by some practices potentially damaging to human and animal health (Goldburg and Naylor 2005; Naylor and Burke 2005) that include passing large amounts of veterinary drugs into the environment (Boxall et al. 2004).

This use has resulted in an increased antibiotic resistance of bacteria in the environment (Petersen et al. 2002; Alcaide et al. 2005; Liyanage and Manage, 2016a; Liyanage and Manage 2017). Moreover, this development has been accompanied by an increase of antibiotic resistance in fish pathogens (Davies et al. 1999; Defoirdt et al. 2011) and increases the possibilities for passage not only of these antibiotic-resistant bacteria but also of their antibiotic resistance determinants to pathogenic bacteria and then to terrestrial animals and human beings (Sorum 2006; Liyanage and Manage 2014).

(a)



(b)

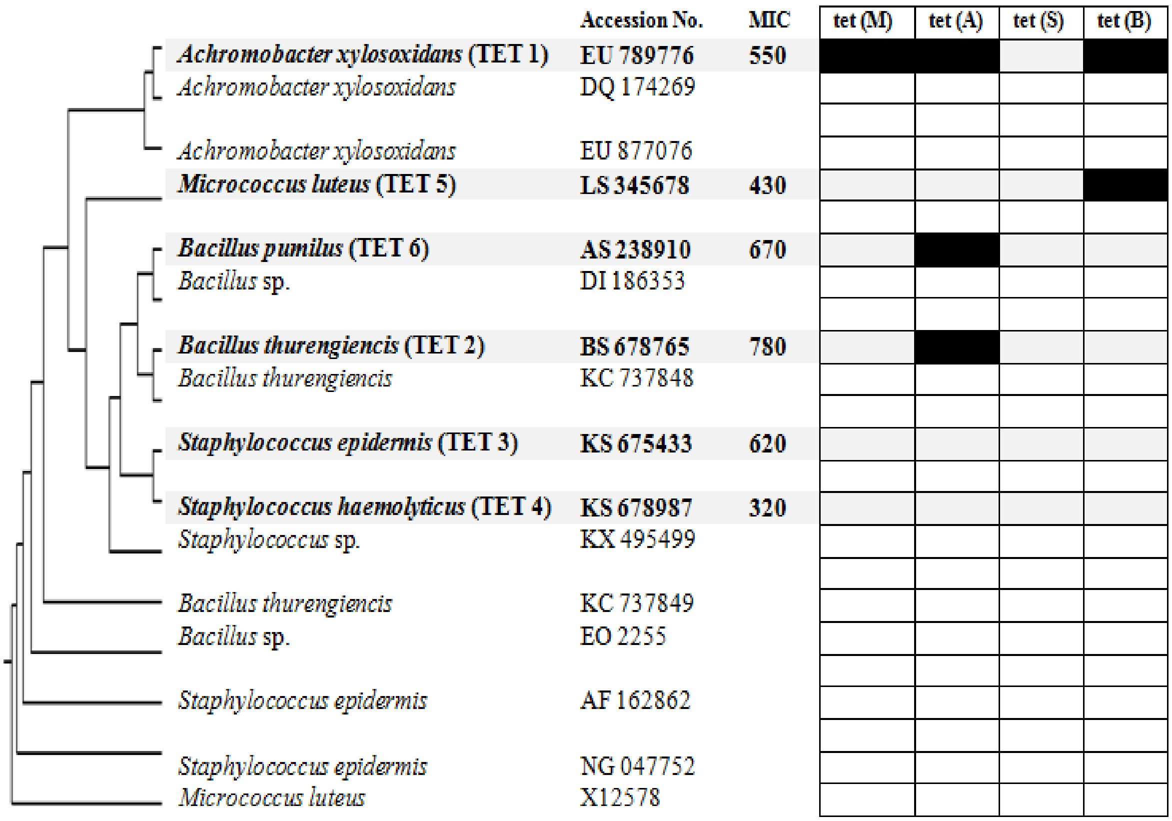


Figure 4. Phylogenetic affiliations with their phylogeny, Minimum Inhibition Concentration (MIC) values, and their resistance genes. (a) OTC resistance bacteria (OCTr); (b) TET resistance bacteria (TETr), The phylogeny was constructed by neighbor-joining method based on Mega 6/ Cluster W from alignment of 16s rRNA gene sequence comparison of antibiotic-resistant bacteria.

However, long-term use and misuse of antibiotics may cause alteration of microbial communities and the generation of drug-resistant strains of bacteria (Subasinghe et al. 2000).

RISK FOR ANIMAL HEALTH

The high detection frequency and concentration of TET are likely due to a large amount of TET used as feed additives and to control diseases in aquaculture sites. Thus the results of the study of Liyanage and Manage (2016b, 2017) agree with several previous studies, which show that TET is resistant to degradation and has sufficient hydrophobicity for transport into aquatic environment (Shah et al. 2014). The study demonstrates that aquaculture farms have been a reservoir of TET, ARB, and ARGs. The TETr bacteria; especially the possible opportunistic pathogens isolated from aquaculture environment and the presence TETr genes, implies an urgent need for constructing a monitoring system for antibiotic usage in aquaculture. Because ARGs and isolated ARB in farm water may lead to problems in the fish diseases and eventually to production losses at the fish farms.

RISK FOR HUMAN HEALTH

Antibacterial agents may disturb the microflora of human intestinal tract and increased risk for certain infections. When people taking an antibiotic for any reason, increased the risk for infections due to particular pathogens become resistant to that antibiotic (Pham et al. 2015). Also increased the frequency of treatment failure and increased the severity of infection as a result of antibiotic resistance and that may result in the prolonged duration of illness, increased the frequency of bloodstream infections, increased hospitalization (Kruse et al. 1994). Also for antibacterial resistant nontyphoid *Salmonella* serotypes and *Campylobacter*, increased morbidity or mortality has been demonstrated (Moges et al. 2014). It is reasonable to assume that the same phenomenon that has been demonstrated for *Salmonella* and *Campylobacter* species can occur with other drug-resistant human pathogens, for which resistant may originate in aquaculture.

ANTIBIOTIC USAGE AND FUTURE

The antibiotic era began in the 1930s, with the discovery and isolation of bactericidal compounds made by actinomycetes fungi. Over the next few decades during what has been called the golden era of antibiotic drug discovery at least 65 antibiotics in nine classes were found and introduced into medical use. However, at present most of the antibiotics lose their effectiveness over time as antibiotic resistance evolves and spread. New antibiotics are more expensive and out of reach for many who need them, especially in low-and-middle-income countries with a high burden of infectious diseases. New agents are not the most important tool in maintaining the global stock of antibiotic effectiveness. Conserving the effectiveness and complementary technologies are vital.

RISK MANAGEMENT OPTIONS

The most effective means to prevent and control the development and spread of antibacterial resistance is to reduce the use of antibiotics by reducing the need for antibacterial treatments (Moges et al. 2014). A regulatory framework at the national level is needed for registration, approval, and control of the use of antibacterial agents in all countries in which antibacterial agents are used in aquatic animals. Production management should include stocking programs and management practices to avoid the introduction of pathogens and to prevent disease outbreaks and should include control measures to be implemented if the disease occurs. WHO estimated that by 2050, antimicrobial resistance will be responsible for 4.7 million deaths in the Asia region (WHO 2015). In Sri Lanka developed the National Strategic Plan (NSP) 2017-2022 with the collaboration of WHO in 2016 (National Strategic Plan-2017-2022). The NSP is developed under five key strategies which are aligned with the strategic objectives of the Global Action Plan. Those strategies are; improve awareness and understanding of antimicrobial resistance through effective communication, strengthen the knowledge and evidence base through surveillance and research, Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures, optimize the use of antimicrobial medicines in human and animal health and prepare the economic case for sustainable investment and increase investment in new medicines, diagnostic tools, vaccines and other interventions. Further studies that provide clear evidence of the link between inappropriate antibiotic use in aquaculture, and antibiotic residues and antibiotic resistance in bacterial pathogens, are needed to develop the appropriate control strategies.

CONCLUSIONS

Use of antibiotics in aquaculture provides a selective pressure that creates reservoirs of drug-resistant bacteria and transferable resistance genes in fish pathogens and other bacteria in the aquatic environment. From the reservoir in the aquaculture environment, some antibiotic-resistant pathogenic bacteria can be transferred to humans, but more importantly, resistance genes from bacteria in the aquatic environment can disseminate by horizontal gene transfer and reach human pathogens. The risk of horizontal gene transfer from fish pathogens and other bacteria in the aquatic environment to human pathogens has not been fully investigated, but it is likely to be significant. 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 antimicrobial agents in this area of animal production, efforts are needed to prevent the development and spread of antimicrobial resistance in aquaculture. These efforts should be focused on improvement of management routines, regulatory control of the use of antimicrobial agents, implementation of prudent use guidelines and monitoring of the use of antimicrobial agents and antimicrobial resistance.

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