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Antibiotics Resistance in Bacteria Strains Isolated From Fish: Potential Health Risk.

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Abstract

Fisheries and aquaculture provide an important source of food and livelihoods for more than one billion people globally. Products from fisheries and aquaculture have sometimes been associated with certain food safety issues. This article reviewed the issues of antimicrobial resistance in aquaculture as documented by some workers. Literature reviewed revealed multiple drug resistance of bacterial strains to commonly used antibiotics. The public health implications of these observations are discussed. Effective use of antimicrobial drugs, authorization of prudent use of veterinary antimicrobial drugs, good aquaculture practices and efficient management of municipal 'waste among, others are recommended to curb the issue of antimicrobial resistance in aquaculture products.

Keywords: Aquaculture, Antibiotic resistance, Bacteria, Public health, Resistance.

1.0 **Introduction**

Aquaculture is currently one of the fastest growing food production sectors in the world (FAO/NACA/WHO,1999). Its increasing global importance is directly related to the contribution it makes to reduce the gap between supply and demand for fish production. FAO (1994) asserted that fish contributes about 60% of the world supply of protein and that 60% of the developing world derives more than 30% of their animal protein from fish. Fish are generally regarded as safe nutritious foods but products from aquaculture have sometimes been associated with certain food safety issues (WHO, 2007). Yunxia *et al* (2001) reported that intensive production of fish increases the likelihood of and severity of parasite and diseases outbreaks, which constitutes a major constraint to aquaculture production. Bacterial agents are among the highly encountered causes of diseases in aquaculture, stressful conditions play important role in establishing and aggravation of the bacterial diseases in fish farms (Paxanelli *et al*,1998; Noga, 2000).

The continuous pollution of the aquatic environment increases the likelihood of infection; untreated wastes are deposited on the grounds, washed away by rainwater and discharged into nearby natural water bodies and ponds (Odiete,1999). Bakare *et al* (2003) observed that water resources have been renderered unwholesome and hazardous to human and other living organisms as a result of water pollution. The toxic substances discharged into water bodies are not only accumulated through the food chain (Odiete,1999) but may also either limit the number of species or produce dense populations of microorganisms (Okafor, 1985). A large number of fish species, both marine and freshwater are potential sources of medically important zoonotic diseases (Acar and Moulin,2006). Some of these zoonoses are highly pathogenic; and the main cause of human infection is the interaction of Man with this organisms both in the consumption of raw or inadequately cooked fish or during processing (Sowumi *et al*,2008; Adedeji *et al*, 2011). In view of the fact that aquaculture is a fast growing food production sector and its increasingly important sources of protein available for human consumption; and from being seen as green industry with great potential and considering the challenges of the bacterial infection, these necessitate the use of antibiotics for treatment and growth promoters in the aquaculture industries. The use of a wide variety of antibiotics in large amount, including non-biodegradable antibiotics useful in human medicines as prophylactic and chemotherapeutic in aquaculture has led to a growing problem for human and animal health and for environment (Daniel,2002). The uncontrollable use of these antibiotics has resulted in the emergence of antibiotics resistant bacteria in aquaculture environments and in the increase of antibiotics resistance in fish pathogens. Recent studies have shown that many antibiotics persist in the sediment and in the aquatic environment for several months following administration (Bjorklund *et al.*,1996; Hirsch *et al* ., 1999; Miranda and Zemelman,2002). The residues of antibacterial agents may affect the sedimentary microbial community and introduce antibiotics resistance in the bacteria (Hektoen *et al*, 1995). McPherson *et al* (1991) observed that individual and multiple antibiotics resistances were associated with antimicrobial use. This issue of antibiotics resistance has stimulated intense debates. The development of antibiotic resistance by pathogenic bacteria is considered to be of one of the most serious risks to human health at the global level. This article reviews the incidence of multiple drugs resistance arose from bacteria strains isolated from aquatic environments and aquaculture products in the tropical environments as documented by some workers.

2.1 Antibiotics and Growth Promoters

Antibiotic is a term often used synonymously with the term Antibacterial. Antibacterial is an agent that inhibits bacteria growth or kills bacteria. Antibacterial are grouped based on the basis of chemical or biosynthetic origin into natural (e.g penicillins produced by fungi in the genus, penicillium), and semisynththetic or synthetic (e.g sulfonamide, the quinolones and oxazolidinones). Another classificationis based on biological activity in which antibacterials are divided into two broad groups; bactericidal agents (i.e kill bacteria) and bacteriostatic agents (i.e slow down or stall bacterial growth). The effectiveness of antimicrobial therapy with antibacterial compounds depends on several factors, these include host defense mechanism, the location of infection, and the pharmacodynamics properties of the bacterial (Pankey and Sabath, 2004). Antibacterial agents can be orally ingested, while intravenous, intramuscular, sub-cutis and topical application are among other means of antibacterial administration. The utilization of antimicrobial has played an important role in treatment and growth promotion in the aquaculture industries (Alexandal *et al*., 2010.)

Tetracycline is a broad spectrum antibiotics used to treat a variety of infection, and is also used as growth promoters in animals. Sulfonamides (Sulfadimethoxine, sulfamethazine, Sulfamethoxazole) are generally used to treat a wide variety of bacterial and coccidial infections in food producing animals and are used as growth promoters. The practice of using antimicrobial agents in fish has been criticized(CDC,2008;Sahu *et al*.,2007); however, intensification of aquaculture has led to the promotion of conditions that favour the use of wide range of chemicals including antibiotics, pesticide, hormones, anaesthetics and various pigments. As in other animals production sectors, antibiotics are used in aquaculture during both production and processing, mainly to prevent (prophylactic use) and treat (therapeutic use) bacterial disease (FAO, 2002). Routine uses of antibiotics as growth promoters is a matter of debate in animal farming industry. In the advance countries of the world, several antibiotics are prohibited for usage in food producing animals. In Canada, for example, the over – the- counter purchase of tetracycline is supported by the existence of a Medicating Ingredients Brochure, which recommends conditions for its use. This is not the case in developing countries where drugs are purchased and used without prescriptions by qualified professional. Drugs approved for aquaculture in some advanced countries of the world are shown in Table 1.

Table 1. Number of drugs approved for aquaculture in the world.

Drug types	Australia	Canada	Europe	Japan	USA
Antimicobials	-	4	7+	27	3
Microbicides	-	4	6 + +	3	1
Anaesthetics	1	2	1 + + +	2	1
Hormones	3	-	-	-	-

+ Amoxicillin, florfenicol, flumequine, oxolinic acid, oxytetracycline, sarafloxacin and sulfadiaznetrimethoprim.

+ +Azamethiphos, bronopol, cypermethrin, emamectin benzoate, hydrogen peroxide and teflubenzuron.

+ + + Tricaine methane sulphonate (MS22)

Sources: Furones and Rodgers (2009).

However, the minimum residue limits are approved for these compounds. Usage of antimicrobial drugs is not controlled in many tropical developing countries.

2.2 Antibiotic Resistance in Aquaculture

Antimicrobials drugs used in aquaculture are usually administered in feed, either compounded during manufacturing or surface-coated onto feed pellets; they are also used in the hatchery as bath medication. The constant assault on the aquatic environments as a result of indiscriminate discharge of untreated waste (pharmaceutical effluent) on to land and water bodies have also exposed aquatic animals to low doses of antimicrobial agents (Lateef,2004). The use of antimicrobial agents in aquaculture has always been subject to Veterinary Medicine Control, wherever such National Control System exists. For example in the United Kingdom, four antibiotics are licensed for use in fish. Oxtetracycline, Oxolinic acid, Amoxicillin and Co-trimazine (trimethoprim+sulfadiazine) (WHO,1999). In some countries, regulations may exist but are not effectively enforced; in others where there is no regulation, farmers use any drugs available in the markets and which may be of poor quality. The problem may lead to evolution of resistance. Bacterial flora of aquaculture products and its environments may be sensitive or resistant to antibacterial depending on the physico-chemical parameters of the environments such as water temperature (T ^{o}C), Total Dissolved Solids(TDS), pH e. t. c (Noga,2000). Resistance or sensitivity must therefore have reference to a specific context. Smith *et al*(1994) reported that the biochemical mechanism by which bacteria display resistance include the production of enzymes that destroy or modify the antibiotic, possession of a permeability barrier that prevent access to the bacterial cell or alteration of the target site that is normally attacked by the antibiotics. Genetic mechanisms by which bacteria acquire resistance include chromosomal mutation and the acquisition of extrachromosomal elements (resistance plasmids). Plasmids-mediated resistance to antimicrobials has been identified in a number of bacterial fish pathogens including *Aeromonas salmonicidia, Aeromonas hydrophila, Vibrio anguillarium, Pseudomonas fluorescences, Pasteurella piscicidia* and *Edwardsilla tarda* (Aoki, 1988), *Yersinia ruckeri*(DeGrandis and Stevenson, 1997). Transferable R-plasmids encoding resistant to Chloraphenicol, Sulfonamides, Streptomycin Trimehoprim and or Tetracycline in Ireland (Aoki, 1997). In Scotland, trasferable R-plasmids were found in 11 out of 40 oxytetracycline-resistant Aeromonas salmonicidia isolates. Transferable resistance was detected to combinations of Oxytetracycline, Streptomycin, Sulfamethoxine and/or trimethoprim (Inglis,1993). Widespread use and abuse of antibiotics especially in hatcheries has also led to the development of multiple drug resistance among microbial populations associated with farmed shrimp production (Brown,1989).

2.3 Antibiotics Resistance in Bacteria Strains Isolated from Aquatic Organisms and its Environments: West African Case Studies.

Evidence has shown that resistant strains of fish pathogens have emerged. Determination of antimicrobial resistance and susceptibility and gross differences between laboratories (Smith *et al*.,1994) render it difficult to quantify. Tsoumas *et al* (1989) observed that the proportion of isolates showing resistance to individual microbials fluctuated considerably overtime. Many workers(Adewoye,2003; Lateef *et al.*,2005;Adedeji *et al*., 2011;Efuntoye *et al*.,2012) have documented cases of multiple drug resistant in bacteria isolated from fish and fish products, cropped from tropical water environments.

In a microbiological study carried out by Lateef (2004) on effluent discharged into natural environment by a pharmaceutical company, he isolated some organisms; *Staphylococcus aureus, Esherichia coli, Proteus vulgaris, Serratia marcescens* and *Pseudomonas aeruginosa*. The organisms were subjected to antibiotics to ascertain the level of antibiotics resistance. High levels of resistance (Table 2) were obtained among the bacteria isolates to antibiotics (50-100%). None of antibiotics tested had 100% activity against all the bacterial isolates.

Table 2. Resistance of bacterial isolates against individual antibiotics[a]

Antibiotics	Bacterial isolates					Cumulative resistance
	Ec	St	Pv	Ps	Sm	
Aug	5(100)	3(60)	ND	3(60)	5(100)	16(64)
Amx	5(100)	5(100)	1(20)	5(100)	4(80)	4(80)
Ofl	4(80)	3(60)	ND	5(100)	1(20)	13(52)
Tet	2(40)	2(40)	2(40)	2(40)	5(100)	3(12)
Nal	3(60)	4(80)	ND	4(80)	4(80)	16(64)
Gen	1(20)	ND	ND	ND	2(40)	15(60)
Cot	2(40)	ND	5(100)	4(80)	5(100)	13(52)
Nit	4(80)	5(100)	5(100)	ND	5(100)	19(76)

[a] No of resistant isolates. (%) in parenthesis; ND, not detected; a total of 25 isolates used, five for each bacterium. Ec(*E.coli*); St(*S.aureus*); Pv(*P.vulgaris*); Ps(*P.aeruginosa*); Sm(*S.marcescens*). See Methods for the abbreviations used for the antibiotics.

Source: Lateef (2004).

This might have resulted as a result of exposure of these organisms to low level of antimicrobial agent seepage into the environment.

Bacterial strains harvested from some healthy *Clarias gariepinus* (Efuntoye *et al*.,2012) sourced from three (3) farms in Ago- Iwoye were subjected to antibiotics sensitivity tests as shown in Table 3.

Table 3: Antibiotic resistance (%) in bacteria isolated from *Clarias gariepinus*

Antibiotics	*E coli*	*Pseudomonas spp*	*Salmonella spp*	*Staphylococcus spp*	*Edwardsiella tarda*
Ampicillin	82.4	63.6	42.9	73.3	0
Amoxcycillin	41.2	54.5	57.1	66.7	0
Chloramphenicol	82.4	36.4	57.1	53.3	0
Ciprofloxacin	0	9.1	0	0	0
Erythromycin	47.1	9.1	85.7	66.7	100
Gentamicin 1	7.6	18.2	71.4	40.0	0
Nalidixic acid	5.9	63.6	14.3	6.7	0
Novobiocin	11.8	9.1	0	6.7	0
Nitrofurantoin	17.6	27.3	28.6	6.7	0
Streptomycin	29.4	36.4	42.9	46.7	0
Sulphamethoxazole	0	9.1	57.1	20	100
Tetracycline	82.4	72.7	28.6	40	0
Ofloxacin	0	0	0	0	0

Source: Efuntoye *et al.,(*2012)

Among the organisms isolated *E. coli* was found to be highly resistant to ampicillin, chloramphenicol and oxytetracycline (82.4%). Majority of the *Pseudomonas aeruginosa* isolated were resistant to ampicillin (63.6%), amoxicillin (54.5%), nalidixic acid (63.6%) and oxytetracycline (72.7%) and noted that most of the *Salmonella sp* were resistant to Erythromycin (85.7%). The exposure of the aquatic animals to low doses of antibiotics for long time for growth promotion and prevention of infection might have resulted in development of antibiotic resistance. Human healthy carrier of some pathogens might have been a contributory factor since some antibiotics implicated are commonly used antibiotics among men folk to treat various diseases or ailment. Sometimes seepage of residue of the antibiotics from the surrounding environment into ponds might have resulted in emergence of antibiotics resistance. Transference of resistant pathogens or resistant genes from human might also be a contributory factor. However, the study observed some isolates that were highly sensitive to Ciprofloxaxin, Novobiocin and Ofloxacin, these antibiotics among others might have not been abused in that environment.

In another study (Adedeji *et al*.,2011) on bacteria isolated from fish sourced from different aquatic environments, multiple drug resistance of four to eight antibiotics were reported among the thirty two strains of bacteria belonging to the genera: *Escherichia, Staphylococcus, Salmonella* and *Streptococcus* as shown in Table 4, tested for their sensitivity to commonly used antibiotics.

Table 4. The multiple drug resistant patterns shown by some bacterial strains to commonly used antibiotics.

Resistance pattern	No of antibiotics	Bacterial strains
4	Nal Aug Cot Amx	#ST
	Cfx Ofl Nfx Cip	*SA
	Nit Nfx Tet Cip	*SA
	Nit Cfx Nfx Tet	**SA
5	Nal Aug Nit Cot Amx	*SA
	Nal Aug Nit Cot Amx	#ST
	Nal Aug Nit Cot Amx	##ST
	Amp Cfx Chl Tet Cip	#EC
	Amp Cfx Amx Tet Cip	##EC
	Nit Cfx Nfx Tet Cip	**SA
6	Nit Amp Cfx Ofl Tet Cip	#SA
	Nit Amp Ofl Nfx Tet Cip	#SA
	Nit Amp Cfx Nfx Tet Cip	##SA
	Nal Tet Aug Nit Cot Amx	*SA
	Nal Ofl Tet Nit Cot Amx	**ST
	Nal Ofl Aug Nit Cot Amx	**ST
	Nal Ofl Tet Nit Cot Amx	##ST
	Nal Gen Tet Aug Cot Amx	##SP
7	Nit Amp Cfx Chl Amx Tet Cip	*EC
	Amp Cfx Chl Ofx Amx Tet Cip	*EC
	Amp Cfx Chl Ofx Amx Tet Cip	**EC
	Nit Amp Cfx Chl Amx Tet Cip	#EC
	Amp Cfx ChlOfx Amx Tet Cip	##EC
	Nit Amp Cfx OflNfx Tet Cip	##SA
	Nal Gen Ofl Tet Aug CotAmx	*SP
	Nal Gen Tet Aug Nit Cot Amx	*SP
	Nal Gen Ofl Tet Aug Cot Amx	**SP,#SP
	Nal Gen Tet Aug Nit Cot Amx	**SP #SP
8	Amp Cfx Chl Cfx Amx Nfx Tet Cip	**EC

EC, E coli; ST, S aureus; SP, Streptococcus, SA, Samonella, * isolates from wild catfish;**isolates from cultured catvfish,#isolates from wild tilapia; ## isolates from cultured tilapia. See Methods for the abbreviations used for antibiotics.

Sources: Adedeji *et al* (2011).

Some of these fishes were captured randomly from natural river that serves as pool for effluent discharge of some plants in urban city of Ibadan. Fishes captured are sold to the public as shown by evidence of many sales points along the bank of this river.

The abuse of antibiotics usage in aquaculture during production and processing mainly to prevent and treat bacterial diseases might have resulted into development of resistance, the discharge of pharmaceutical and chemical wastes into natural environments, water bodies and ponds inclusive might have exposed aquatic organisms to low doses of antibiotics thereby resulting in drug resistance.

3.0 Potential Human Health Risks

The public health hazards related to antimicrobial use in aquaculture include the development and spread of antimicrobial resistant bacteria and resistant genes and the occurrence of antimicrobial residues in products of aquaculture. There are lot of food safety issues associated with farmed and captured finfish, particularly biological and chemical contamination that may occur during harvesting and processing. Many workers (Ervik, 1994; Midtvedt and Lingas, 1992; Sandaa *et al*.,1993) have argued that the use of antimicrobials in aquaculture is associated with risks for the therapy of human infections. In temperate climates few bacteria pathogens of farmed fish are capable of infecting human (WHO,1999) but in warmer climates, bacteria pathogenic to fish are acclimatized to temperature much nearer to that of human body (Noga, 2000) and may be capable of surviving in the human gut. *Aeromonas hydrophila* and *Edwardsiella sp* are established to be important fish pathogens in the warmer countries but in recent study carried out by Tiamiyu *et al* (2011) some strains of bacteria of genera: *Bacillus, Proteus, Pseudomonas, Klebsiella, Streptococcus, Salmonella, Staphylococcus, Micrococcus, Serratia* and *Escherichia* were isolated from fish and fish products cropped in feral and cultured ponds in some aquatic environments in Ibadan, Southwest, Nigeria. Among these pathogens are coagulative positive species Staphylococcus aureus which are widely believed to be the broadest pathogenic heterogenous groups of Staphylococcus aureus and Coagulative Negative Staphyloccus(CNS) regarded as less pathogenic, but said to have emerged as nosocomial pathogens in immunocompromised individuals(Ziebhur,2001). Ziebuhr(2001) also reported that Staphyloccocci, the gram positive facultative anaerobic bacteria, are widespread among mammalians where they belong to the healthy microflora of skin. The pathogenicity of these bacterial strains isolated on fish is yet to be established. The transfer of resistance to human pathogens and gut bacteria is of major concern. Such transfers probably happen easily and often, as argued by several studies that the use of antimicrobials in aquaculture is associated with risks for the therapy of human infections(Midtvedt and Lingas,1992; Sandaa *et al*.,1993; Ervik *et al*.,1994). Bacteria have the genetic ability to transmit and acquire resistance to drugs which are utilized as therapeutics agents, such a fact is a cause for concern, considering the number of patients in hospital whose immunity have been compromised due to new bacterial strains which are multiresistant. Less effective drugs can result in high mortality. Many workers (Malik and Ahmed,1994; Silva and Hoffer, 1993; Lateef,2004;Adedeji *et al*.,2011; Efuntoye *et al*,2012) have established high level of resistance to antimicrobial agents, a reflection of misuse or abuse of these agents in the environment(Umoh *et al* .,1990; Lateef,2004). The antimicrobial usage in human medicine, veterinary medicine, animal production, fish production and food technology has impacted the phenomenon of microbial resistance due to the failure of users to adhere to tenets of antimicrobial usage. The animal, human and environment interface have no barriers; people, animal (food animals and pets) and food products move rapidly across the regions, raised the risk of the spread of antimicrobial resistance worldwide. Besides the clinical consequences, equally serious ecological and epidemiological effects result from antimicrobial resistance (Rice,2007).

4.0 Conclusion

Resistance to antimicrobial is becoming increasingly widespread without any plausible association with the use of these drugs, it is necessary to seriously consider strategies to prevent the emergence, re-emergence and dissemination of antimicrobial resistant bacteria. This reviewed article provides valuable information to the ministry of medical services, public health organization, ministry of agriculture, fishery departments and other relevant agencies in making policy decisions aimed at reducing microbial contamination of fish and water, management of effluents discharged by industries and avoidance of indiscriminate use of antibiotics. There is need for research on antibiotics susceptibility surveillance in the aquatic environments where fish and water are obtained for human consumption.

5.0 Recommendations

To minimize the potential resistance effects of antimicrobial agents use in food producing animals, it is important to provide effective use of veterinary antimicrobial drugs in veterinary medicine by maintaining their efficacy. The consumers of animal food origin (milk, egg, meat, fish) have to be protected health-wise by preventing as far as possible the direct transfer of resistant microorganism or resistance determinants within animal populations and from food animal to human.

The National Regulatory Authority which are responsible for authorization of prudent use of veterinary antimicrobials drugs in food producing animals should develop up to date guidelines on data requirements for evaluation of veterinary antimicrobial drugs applications.

The use of antibiotics in fish farming should be discouraged, the developments of vaccines and immunostimulants incorporated in the feed and general preventive health efforts have to be urgently considered.

Good Aquaculture Practices (GAP) should be embraced, the producers should be responsible for preventing diseases outbreaks and implementing health and welfare programmes on their farms.

Extension Information on good husbandry and pond management on the prevention of diseases should be disseminated through small workshops and written materials in appropriate languages.

Measures should be put in place to avoid the release of harmful substances into the environment, and this should be incorporated in the design, operations, maintenance and management of industrial plants.

6.0 References

Acar J. F and Moulin, G (2006): Antimicrobial resistance at farm level. Revue Scientifique et Technique(International Office of Epizootics)25(2):775-92

Adedeji, O. B; Tiamiyu, A M; Emikpe, B. O (2011): The Antibiotics Resistance Patterns of Bacterial flora of fish from different Aquatic Environment from Ibadan, Southwest, Nigeria, Advances in Environmental Biology,5(8):2039-2047.

Adewoye,S.O and Lateef, A(2003): Evaluation of the Microbiological Characteristics of Oyun River- a Polluted River in North central Nigeria. *Pollution Research*. **22**.457-461

Alexander CP, Kirubakaran UW, Michael RD(2010); Water soluble
fraction of Tinospora lordifolia leaves enhanced the nonspecific immune mechanism and disease resistance in Oreochromis mossabicus. analysis in marine fish. J Virus Res 1989; 99(7): 988-996.

Aoki, T (1988): Drug resistant plasmids from fish pathogen. Microbiological sciences 5, 219-223

Aoki, T (1997): Resistance plasmids and the risk of transfer. In: Bermoth E. M ed. Furunculosais multidisciplinary fish disease research: London. Academic press. 1997:433-440

Bakare, A.A; Lateef, A; Amuda, O and Afolabi, R. O(2003): The Aquatic Toxicity and Characterization of chemical and microbiological constituents of water samples from Oba River, Odo-Oba, Nigeria. Asian Journal of Microbiological, Biotechnology and Environmental Sciences 5, 11-17

Bjorklund, H; Bergh, R; Bylund, C.M. I(1991):Residues of oxolinic acid and Oxytetracycline in fish and sediments from farms. Thesis Bjorklund, h Oxytetracycline and Oxolinic acid as antibacterials in aquaculture-analysis, pharmacokinetics and environmental impacts, Departments of Biology Abe Akademi University, Finland.

Brown, J. H (1989): Antibiotics their use and abuse in aquaculture. World aquaculture,20:34-43

Centers for Disease Control and Prevention.(2002): Outbreak of multidrug-resistant Salmonella Newport—
United States, January- April 2002. Morbidity and Mortality Weekly Report 51(25):545-8. November 14, 2008.

Daniel, P (2002): A review about available treatments for sea farming. In: Workshop on Fish Farming and Health Management Handbook, Trieste (Italy), 16 October 2002. European Aquaculture Society Publ.,164, p.15-21

DeGrandis S.A and Stevenson, R.M W(1997): Antimicrobial susceptibility patterns and R plasmid- mediated resistance in fish to the pathogen Yersinia ruckeri: Antimicro agents and chemotherapy. 27: 938-942

Efuntoye, M.O; Olurin, K. B; Jegede, G.c (2012): Bacteria flora from healthy Clarias gariepinus and their Antimicrobial Resistance Pattern. Advance journal of food Science and Technology 4(3):121-125,2012.

Ervik, A(1994): Impact of administering antibacterial agents on wildfish and blue mussels(Mytilis edulis) in the vicinity of fish farms. Disease of aquatic origin. 18:45-5.
FAO(1994): Food and Agriculture Organization of the United Nations: marine Fisheries:Review of state of the world Fishery CircularNo 920, Rome.
FAO(2002): The state of world fisheries and aquaculture. ISBN 92-5- Fish Pathol.,17.p.251-260.
FAO/NACA/WHO(1999): Food Safety Issues Associated with products from Aquaculture.Report of a joint FAO/NACA/WHO study Group. WHO Technical Report series. 883
Furones, M. D; Rodgers, C.J. (2009): Antimicrobial agents in aquaculture practice, needs and issues. Ins:Rogers. C.(ed).Basu reo B,(ed). The use of veterinary drugs and vaccines in Mediterraneaean aquaculture.Zaragoza: CIHEAM.2009.p.41- 59(Options Mediterrranean:Serie A Seminaires)
Health Management Handbook, Trieste (Italy), 16 October2002. European Aquaculture Society.
Hektoen, H; Bergeod, A; Habererklaus; KratzKarl-ludwig(1995): Persistence of antibacterial agents in marine sediments, Aquaculture 1995;133:175-84
Hirsch, R; Terries Thomas,Habererklaus, KratzKarl-udwig(1999): Occurrence of antibiotics in the aquatic environment. Sci Total Environ(1999)(12january);225(1-2)109-18
Inglis V. (1993): Resistance of Aeromonas slamonicida to amoxicillin. Journal of fish diseases 16:389-395.
Lateef, A., Oloke, J.K. and Gueguim Kana, E.B. (2004). Antimicrobial Resistance ofBacterial strains isolated from Orange Juice products. *African Journal of Biotechnology* **3**: 334-338
Lateef, A; OLoke,J.K and Guegium Kana, E. B(2005): The prevalence of bacterial resistance in clinical, food, water and some environmental samples in Southwest Nigeria. Environmental Monitoring and Assessment 100:59-69
Malik, A and Ahmad, M (1994): Incidence of Drug and Metal Resistance in E. Coli strains from Sewage Water and soil, Chemical and Environmental Research 3, 3-11.
Mcphearson jr R. M; Depaola, A; Zywno S.R; Motes jr M.L; Guarino, A.M (1991): Antibiotics resistance in Gram negative bacteria from culture catfish and aquacukture ponds. Aquaculture 1991;99(3/4):203
Midtredt, T and Lingaas E(1992): Putative Public health risks of antibiotics resistance development in aquatic bacteria, In:Michel C, Alderman D J.eds. Chemotherapy in Aquaculture: From Theory to Reality, Paris, office international de Epizootics,1992:302-314
Miranda C.D Zemelmar Raul (2002) : Bacteria resistance to oxytetracycline in Chilean Salmon farming. Aquaculture 2002 (23 september); 212 (1-4): 31-
Noga E.J. (2000): Fish disease diagnosis and treatment (Iowa: Iowa State University Press)
Odiete, W. O (1999): Environmental Physiolology of Animals and
Pollution. Diversified Resources Ltd Lagos,1st ed. Pp187- 219ISBN978-028957-7.
Okafor, N(1985): Aquatic and Waste Microbiology,1st Ed., Fourth
Dimension Publishing Company Ltd. Enugu, pp 187-219. ISBN9781561270S
Pankey, G. A and Sabath, L. D (2004): Clinical relevance of bacteriostatic versus bactericidal mechanisms of action in the treatment of Gram positive bacterial infections''Clin infect Dis. 38(6)870
Paxanelli, G.C.; Eiras, J.C., and Takemoto, R.M. (1998): Doencas de peixes: profilaxia, diagnostics etratamentos Eduem (ed) pp. 125- 166. Nupleia, Maringa, Brazil.
Rice, L. B(2007): Emergin issues in the managements of infection caused by multidrug resistant gram negative bacteria. Clere. Clin. J Med. 2007, 74(suppl 4), 512-520
Sahu, S., Das, B.K., Mishra, B.K., Pradhan, J. and Sarangi, N., 2007. Effect of *Allium sativum* on the immunity and survival of *Labeo rahita* infected with *Aeromonas hydrophila*. *J. Appl. Ichthyol*.**, 23:** 80-86.
Sandaa, R.A; Torsvik,V.L; Goksoyr, J(1993):Transferable drug resistance in bacteria from fish farm sediments. *Canadian journal of microbiology*.38:1061-1065
Salyers, A.A(1995): Antibiotics resistance transfer in the mammalian intestinal tract.
Silva, A.A.L and Hoffer, E(1993): Resistance to antibiotics and heavy metals in *E coli* from marine environment. *Environmental Toxicology and Water Quality* **8**, 1-11
Smith, P; Henry,M; Samuelsen, O.B(1994): Bacterial resistance to
antimicrobial agents used in fish farming ; a critical evaluation of method and meaning. Annual review of fish diseases. 4:273-313

Sowunmi. A.A; Okunubi, M.A and Efuntoye, M.O (2008): Occurrence of bacteria in gill and buccal cavity of Clarias gariepinus (Burchell, 1822) and Tilapia zilli (Gervais) from Lekki lagoon, Southwest Nigeria Technique (International Office of Epizootics)25(2):775-92.

Tiamiyu, A.M; Emikpe, B. O; Adedeji, O. B(2011): Isolation and identification of aerobic Bacteria Flora of the skin and stomach of wild and cultured Clarias gariepinus and Oreochromis niloticus from Ibadan Southwest Nigeria. Journal of applied sciences research,7(7):1047-1051

Tsoumas, A Alderman, D. J;Rodgers C.J(1989): Aeromonas salmonicida; development of resistance to 4-quinolone antimicrobials. Journal of fish disaeses.12:493-507

Umoh, V.T; Adesiyun, A.A and Gomwalk N.E (1990): Antibiogram of Sterphylococcal Strains isolated from Milk and Milk Products, Zentralblatt fun veterina-medizin(B) 37,701-706

WHO(1999):Joint FAO/NACA/WHO study group on food safet issues associated with products from aquaculture. Who Technical Report Series,p883.

WHO (2007): Food safety issues associated with products fromAquaculture. Report of a Joint FAO/NACA/WHO study Group, WHO Technical reprint Series: 883 + Geneva. Pany

Yunxia, Q;Jiazhog, S; and Guoliang, W(2001): A review of principal bacterial disaeses of mariculture fish. Transact.Oceanol.Limnol.,2:78-87

Ziebuhr, W(2001): Staphylococcus aureus and Staphylococcus epidermidis: Emerging pathogens in Nosocomial infections, contribution to Microbiology, 8:102-107