CHAPTER

4 Current trends of antimicrobials used in food animals and aquaculture

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4.1 Introduction

Antimicrobials are used globally both for humans and animals to obviate and treat contagious diseases (O'neill, 2014). Furthermore, in some countries, antimicrobials are used in animal breeding as growth promoters (Flórez et al., 2017). Antimicrobial agents are one of the medicinal innovations of humanity that allows us to cure both human and veterinary infections of microbes. Since the 1940s, several antimicrobials have contributed significantly for prevention, restriction, and cure of contagious diseases in animals. Low- and subtherapeutic antimicrobial dosage plays a very important role in improving feeding proficiency, stimulating animal growth, disease avoidance, and control (Magouras et al., 2017).

There are four ways in which substances expressing antimicrobial activity are used in animals. Therapeutic usage of antimicrobials is considered to prevent existing microbial diseases, usually used for individual animal cure. It involves testing of each infected animal, which involves laboratory examination, determining the microbes and antimicrobial sensitivity testing. Antimicrobials are administered either orally or via inoculation only to animals showing symptoms of that particular illness. The dosage that is injected is related to both the type of animal and the severity of illness. Metaphylaxis includes prior medication to the whole animal group that might lessen the numbers of sick or deceased animals. It might also reduce the antimicrobial dosage required for the treatment of huge numbers of the symptomatically sick populace, therefore treatment expenses are also reduced. Antimicrobial prophylactic application exists for individual and animal groups. It is generally used for operative prophylaxis in animals. In cattle, the prophylactic intramammary injection of antimicrobial agents at the end of the suckling phase prevents mastitis. In swine and cattle husbandry, antimicrobial prophylactic usage occurs at significant time periods like weaning. Antimicrobial prophylaxis usage is critical in numerous pigs and cattle herds. In its absence, continual breathing and enteral illnesses in

Antibiotics and Antimicrobial Resistance Genes in the Environment. https://doi.org/10.1016/B978-0-12-818882-8.00004-8

the byres and piggeries cannot be effectively controlled. Growth promotion also involves antimicrobial usage in food animals. Antimicrobial growth promoters were first endorsed in the mid-1950s.It was revealed that small and subtherapeutic dosage of antimicrobials like penicillin, procaine, and tetracycline (1/10 to 1/100 the quantity of curative dosage), given to animals in food, could increase the food/mass ratio for chickens, pigs, and cows. All substances used to stimulate growth are certified on the base of European Union (EU)—wide rules (guideline 70-524-EWG). These regulations narrate the usage of the particular substances in various animals in accordance to animal's age, maximal and minimal antimicrobial consumption in mg/kg food. Formerly, just four substances were permitted in the EU, having certified growth promotions with antimicrobial functions. These were flavophospholipol, monensin—Na, salinomycin—Na, and avilamycin. In 1996, the glycopeptide-avoparcin usage as a growth promoter was prohibited. Cross-resistance to glycopeptides (vancomycin; teicoplanin), macrolides (erythromycin; clarithromycin) and streptogramins (dalfo/quinupristin) was the major reason for banning them (Ungemach, 1999; Schwarz et al., 2001).

The widespread and inappropriate utilization of antimicrobials in food animals are contributing factors for the emergence and spread of antimicrobial resistance (AMR). Diseases have become untreatable due to the resistance against therapeutic agents. This also poses a risk to public health through potential transfer of resistance genes to human pathogens. Both pathogenic and commensal microbes are exposed to antimicrobials and in response AMR develops. It has been detected that microbes develop resistance by any of the four mechanisms: through drug inactivation or its modification, alteration in the drug target site, modification in the metabolic pathways to overcome drug effects, and by minimizing entry and promoting active efflux of the drugs (Sharma et al., 2018). Microbes can develop antimicrobial resistance by mutating existing genes (vertical gene transfer) or by obtaining new genes from the environment, other spp., or strains (horizontal gene transfer) (Jeters et al., 2009). Resistance between bacterial spp. has been seen through antibiotic-resistant genes and includes among the primary genes leading to AMR: blaTEM genes for the antibiotics (penicillin, amoxicillin, ampicillin) (Bailey et al., 2011); van for glycopeptides (avoparcin, vancomycin) (Leavis et al., 2003); erm gene cluster for macrolides (erythromycin, tylosin, tilmicosin, kitasamycin, oleandomycin) (Ramos et al., 2012); vatD, vatE, erm gene cluster, satA for streptogramins (virginiamycin, quinupristin-dalfopristin) (Ramos et al., 2012); sul genes for sulfonamides (sulfisoxazole, sulfadimethoxine, sulfamethazine) (Cain and Hall, 2012); tet genes for tetracyclines (chlortetracycline, oxytetracycline, doxycycline) (Ramos et al., 2012); rgpA—F, mbrA—D genes for polypeptides (bacitracin) (Cain and Hall, 2012); and cmaA, floR, fexA, fexB, cfr, cat gene for amphenicols (chloramphenicol (Cain and Hall, 2012).

4.2 Global consumption of antimicrobial trends in food animals

Global utilization of antimicrobials in the production of food animals has been estimated at 63,151 ($\pm$1560) tons in 2010 and it is estimated to increase by 67% to 105,596 ($\pm$3605) tons by 2030.Two-thirds (66%) of global antimicrobial consumption growth (67%) is due to the increasing number of animals raised for food production. The remaining third (34%) is due to a shift in farming practices. It is expected that the larger section of animals to be raised by 2030 will be via intensive farming. Roughly 46% of antimicrobial consumption growth by 2030 in Asia is likely due to shifts in production systems. By 2030, antimicrobial consumption in Asia is predicted to be 51,851 tons. It represents 82% of the current global consumption of antimicrobials in food animals in 2010.

In 2010, China (23%), the United States (13%), Brazil (9%), Germany (3%), and India (3%) were the five countries having substantial shares of global antimicrobial consumption in food animal production. By 2030, it is expected that this ranking will be China (30%), the United States (10%), Brazil (8%), India (4%), and Mexico (2%). Five countries with the greatest projected percentage increases in antimicrobial consumption by 2030 are expected to be Myanmar (205%), Indonesia (202%), Nigeria (163%), Peru (160%), and Vietnam (157%). At the present time, China and Brazil are among the large-scale consumers of antimicrobials. But these are not the countries with the rapid projected increases in antimicrobial consumption. This shows that these two countries have already begun moving toward more escalated livestock production systems using antimicrobials to sustain animal health and increase productivity. Antimicrobial consumption for animals in the BRICS (Brazil, Russia, India, China and South Africa) countries is supposed to grow by 99% by 2030.

4.3 Frequent trends of use of antimicrobials in the treatment of infectious and contagious diseases in food animals

4.3.1 Use of antimicrobials in pigs

Pig weaning is a slow progression that starts at almost 3 months of age and shows the transfer of piglet dependence from lactate to other foodstuffs. But in a majority of developed nations pig weaning is a rapid progression taking place earlier in life, at the age of 19–25 days. It is frequently related to increased risk of stomach dysfunction and dysentery. Pigs eating feed containing antimicrobials showed no symptoms of gastrointestinal impairment at any point, while naturally lactate controls developed dysentery (Li et al., 2013). With antimicrobial usage, there was high day-by-day mass growth in contrast with lactate controls. The streptomycin repeatedly used for pig weaning from delivery to 28 days of age resulted in 8% mass increase compared to natural pigs of 56 days weaning time. Similarly, Aureomycin, Terramycin (oxytetracycline), and penicillin enhanced the swine growth by 10% (Li, 2017). Antimicrobials used are listed in Table 4.1. Specifically, in chicken and pig farming, antimicrobial usage has become a basic part of animal feeds. In the United States, more than a thousand experiments were performed from 1950 to 85. From the results, it was observed that antimicrobials were the efficient agents for feed and growth improvement in adult pigs, as well as the whole growth-finished phase, and reduced death and disease conditions mostly in juvenile pigs. The death rate can be doubly high in the farm environment compared to research locations where the amenities are usually clean, the disease load is less, and the atmosphere is less traumatic (Luecke et al., 1951). The advantageous effects of antimicrobials on body mass growth were accompanied by improved feed consumption effectiveness, enhanced desire for food, and extra common exterior of the fur hair and hide. Thus, antimicrobials have been used as a feed preservative globally for many years. The extent of the improvement in growth rate is based on the type of antimicrobial, nourishment stage, farm atmosphere, and swine conditions (Cromwell, 2002).

4.3.2 Use of antimicrobials in goats and sheep

Research has provided information on antimicrobial use in livestock spp., including cattle and swine, but there is little information on drug use practices for sheep and goats in different countries (Acar et al., 2000; Menzies, 2000). In these countries they are considered as minor spp. They are food-producing animals that do not have a large economic footprint. They are not often targeted for drug

Table 4.1 Antimicrobial use for treatment of diseases in pigs.

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
Gastrointestinal tract	Edema disease	*Escherichia coli*	Trimethoprim, sulfonamides, aminopenicillins
	Pneumonia (bronchopneumonia) (Porcine enzootic - pneumonia)	*Streptococci* *Pasteurella multocida* *Mycoplasma hyopneumoniae*	Benzylpenicillin, trimethoprim, sulfonamides Tiamulin, lincomycin, tetracyclines
Reproductive tract	Balanoposthitis	*Actinobaculum suis*	Benzylpenicillin, aminopenicillins
	Metritis (endometritis)	Coliforms, Gram-positive bacteria	Trimethoprim, sulfonamides, benzylpenicillin
Kidneys and urinary tract	Urinary tract infection (Cystopyelonephritis)	*Actinobaculum suis*	Benzylpenicillin, aminopenicillins
	Inflammation of the bladder (Cystitis)	*E. coli*	Trimethoprim, sulfonamides, aminopenicillins
Respiratory tract	Progressive atrophic rhinitis (Soontornvipart, Kohout et al.)	Toxigenic *P. multocida*	Tetracyclines, trimethoprim
	Pleuropneumonia	*Actinobacillus pleuropneumoniae*	Benzylpenicillin, tiamulin, tetracyclines
	Dysentery	*Brachyspira hyodysenteriae*	Tiamulin (The Finnish Food Safety Authority, 2018)
Central nervous system	Meningitis	*Streptococcus suis*	Benzylpenicillin, aminopenicillins
Musculoskeletal system	Lameness	*S. suis*	Sulfonamides, cephalosporins, aminoglycosides
	Arthritis	*S. suis*, *Mycoplasma hyosynoviae*	Penicillins, lincosamide, tylosin
Mammary gland	Postpartum dysgalactia syndrome (PPDS)	Gram-negative bacteria (mostly *E. coli*)	Trimethoprims, sulfonamides, aminopenicillins
	Chronic mastitis	Gram-positive bacteria	Benzylpenicillin, aminopenicillins (De Briyne et al., 2014a)
	Acute mastitis	Gram-negative bacteria	Trimethoprim, sulfonamides, aminopenicillins (The Finnish Food Safety Authority, 2018)

development and approval. Additionally, the market for drug use is small, resulting in limited financial commitments from pharmaceutical companies. With sparse clinical data generated in North America supporting drug use, it is difficult to license drugs for use in these species. Veterinarians and sheep producers therefore have a limited selection of licensed drugs (Navarre and Marley, 2006). It is thought that much of the drugs used is extra-label drug use (ELDU), which means usage is not in accordance with information mentioned on its label, package insert, or product monograph. Penicillin, tetracycline, oxytetracycline, and florfenicol are extra-label drugs generally used (Fajt, 2001).Antimicrobials used in goats and sheep are listed in Table 4.2.

4.3.3 Use of antimicrobials in cattle and cows

Cattle production is the third largest animal farming in the world (approximately 65 million globally), after swine and poultry (Food et al., 2014). China (6.7 million), Brazil (9.6 million), the United States (US) (11.4 million), the 28 member countries of the European Union (7.5 million), and India (4.5 million) are the fundamental cattle-producing countries in the world, resulting in an excess of one billion cattle population in 2015 (Ali et al., 2016). Cattle raising at massive levels normally involves moving animals from cow-calf systems (a permanent herd used to produce young beef), to back grounding (postweaning intermediate feeding, normally forage-based diets) and feedlot (a building where livestock are fattened for market, usually with high-energy grain-based diets). For the treatment and prevention of diseases in cattle and cows, antimicrobials can be administered in live cattle at any developmental stage (Podberscek, 2009). In the husbandry environment, cattle can be more prone to endemic pathogens. These pathogens are normally neglected, causing severe damage to animal health, and affecting herd growth and farm productivity. The chances of transmission of diseases cause significant economic pressure for antimicrobial use against bovine infectious diseases (Radostits et al., 2006; Van Epps and Blaney, 2016). A number of the antimicrobials being used for the treatment of infections in cattle and cows are mentioned in Table 4.3. Commonly used antimicrobials for treatment of diseases in cattle and cows are trimethoprim/sulfonamides, oxytetracycline, benzylpenicillin, and polymyxin B (The Finnish Food Safety Authority, 2018).

4.3.4 Use of antimicrobials in horse

Meat is one of the major sources of nutrients in human food, for its contribution of high-biological-value protein. Recently, there has been an interest in meat from alternative sources, other than bovine, swine, and poultry. The main producers of horsemeat are China, Kazakhstan, Mexico, Russia, and Argentina, while Mongolia, Switzerland, Italy, Kazakhstan, and Russia are the largest consumers (Vanegas Azuero and Gutiérrez, 2016). It is very challenging to estimate the antimicrobial use in horses. Deciding the volume of antimicrobials to be used in horses in most countries is difficult, if not impossible. As a result, antimicrobials administration strategy and estimation of antimicrobials usage is difficult. There are insufficient answers to the questions of "how much" and "how are" these antimicrobials are administered in horses (Weese, 2015). The major spp. of bacteria detected at the onset of instillation were *Staphylococcus aureus*, *Streptococcus equi* subsp. *Zooepidemicus*, *Acinetobacter lwoffii*, *Staphylococcus xylosus*, *Staphylococcus vitulinus*, *Enterobacter agglomerans*, *Flavimonas oryzihabitans* and *Staphylococcus sciuri* (HIDAKA et al., 2015). Aminoglycosides (e.g., gentamicin, or amikacin) are concentration-dependent bactericidal drugs, therefore the higher the drug

Table 4.2 Antimicrobials use for treatment of diseases in goats and sheep.

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
Gastrointestinal tract	Colibacillosis	Enterotoxigenic *Escherichia coli*	Broad-spectrum antimicrobials
	Salmonella dysentery	*Salmonella typhimurium*	Broad-spectrum antimicrobials
	Abomasitis	*Clostridium* spp.	Oral penicillins
	Coccidiosis	*Eimeria* spp.	Salinomycin, decoquinate, amprolium, and sulfonamides
Reproductive tract	Enzootic abortion of ewes	*Chlamydophila abortus*	Tetracycline, oxytetracycline, tylosin
	Campylobacter abortion	*Campylobacter jejuni*, *Campylobacter fetus* spp.	Oxytetracycline, sulfamethazine penicillin G, streptomycin, tetracycline and tylosin
	Listeria abortion	*Listeria monocytogenes*	Oxytetracycline
	Toxoplasma abortion	*Toxoplasma gondii*	Decoquinate
	Salmonella abortion	*S. typhimurium*, *salmonella abortusovis*, *salmonella dublin*	Broad-spectrum antimicrobial
	Leptospira abortion	*Leptospira hardjo*, *leptospira Pomona*	Penicillin G, streptomycin, tetracyclines
	Brucella ovis ram epididymitis	*Brucella ovis*	Dihydrostreptomycin with oxytetracycline
Respiratory tract	Pneumonic pasteurellosis	*Mannheimia haemolytica*, *Pasteurella multocida*	Tilmicosin, oxytetracycline, ceftiofur, florfenicol
	Pasteurella septicemia (Sheep)	*Bibersteinia trehalosi*,	Tilmicosin
	Necrotic laryngitis	*Fusobacterium necrophorum*	Penicillin G, oxytetracycline
	Mycoplasma pneumonia	*Mycoplasma arginine*, *Mycoplasma ovipneumoniae*	Tylosin, oxytetracycline
Kidneys	Enterotoxaemia	*Clostridium perfringens* type C and D	Oral virginiamycin, Penicillin G
Urinary tract	Leptospirosis	*Leptospira interrogans*	Dihydrostreptomycin, oxytetracycline
	Cystitis	*Corynebacterium renale*, other spp.	Broad-spectrum antimicrobials
Musculoskeletal system and foot	Contagious foot rot	*Dichelobacter Nodosus*, *F. necrophorum*	Oxytetracycline

Table 4.2 Antimicrobials use for treatment of diseases in goats and sheep.—cont'd

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
	Foot scald	*F. necrophorum*	Zinc sulfate foot bath
	Polyarthritis	*Chlamydophila pecorum*	Oxytetracycline
	Polyarthritis (goats)	*Mycoplasma mycoides* (other *Mycoplasma* spp.)	Oxytetracycline, tylosin
Mammary gland	Gangrenous mastitis	*Staphylococcus aureus*, *M. haemolytica*	Tilmicosin
	Contagious agalactia	*Mycoplasma agalactiae*, *Mycoplasma mycoides*	Tetracyclines, tylosin
	Subclinical and clinical mastitis	*S. aureus*, *M. haemolytica*	Tilmicosin, cloxacillin, cephapirin,
Central nervous system	Bacterial meningitis	Many spp.	Broad-spectrum antimicrobials
	Listeriosis	*L. monocytogenes*	Oxytetracycline, penicillin G
Oral cavity	Tooth root abscess	Many spp.	Oxytetracycline, florfenicol
	Actinobacillosis	*Actinobacillus lignieresii*	Sodium iodide
	Actinomycosis	*Actinomyces bovis*	Sodium iodide, sulfadimethoxine, isoniazid
Eyes	Pinkeye (infectious keratoconjunctivitis)	*Chlamydia psittaci*, *Mycoplasma conjunctivae*, *Neisseria*	Spiramycin, oxytetracycline, tiamulin
Skin	Secondary infection of contagious ecthyma (Benkendorff)	*S. aureus*	Tilmicosin, oxytetracycline, ampicillin
	Dermatomycosis (lumpy wool in sheep	*Dermatophilus congolensis*	Oxytetracycline

concentration, the greater the bactericidal effect use against skin, subcutaneous tissue, eye, and urinary tract infections in horses (Papich, 2001; Williams and Pinard, 2013; Carapetis et al., 2017). Beta-lactam antibiotics such as penicillins, potentiated aminopenicillins, and cephalosporins are slowly bactericidal and used for the treatment of urinary tract, skin, subcutaneous tissue, and respiratory tract infections (Papich, 2001; Gordon and Radtke, 2017b; Wilson, 2001). A summary of the major antimicrobials used in horses is provided in Table 4.4.

4.3.5 Use of antimicrobials in poultry

Poultry is one of the world's most popular food industries. Poultry refers to the breeders and production animals of broilers, chickens, and turkeys. Chicken is the most frequently farmed spp., producing more than 90 billion tons of chicken meat per year (Agyare et al., 2018). Most countries use a wide variety of

Table 4.3 Antimicrobials used for treatment of diseases in cattle and cows.

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
Gastrointestinal tract	Coccidiosis	*Eimeria*	Trimethoprim, sulfonamides
	Diarrhea (neonatal diarrhea) Diarrhea (in preweaning calves)	*Escherichia coli* Several viruses, bacteria	Trimethoprim, sulfonamides
Respiratory tract	Bovine respiratory disease (BRD)	*Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, *Ureaplasma* sp. *Mycoplasma* sp.	Oxytetracycline, Benzylpenicillin, macrolides
	Ovine respiratory disease (pneumonia)	*M. haemolytica*, *Pasteurella multocida* mycoplasma	Benzylpenicillin, oxytetracycline
Reproductive tract	Acute metritis	*Trueperella pyogenes*, *E. coli*, *streptococci*, *staphylococci*	Benzylpenicillin, oxytetracycline
Urinary tract	Cystitis	*Corynebacterium renale*, *E. coli*	Benzylpenicillin
Musculoskeletal system	Arthritis	*T. pyogenes*, *E. coli*, *Mycoplasma bovis* other bacteria	Benzylpenicillin, oxytetracycline
	Cellulitis, Bursitis	*T. pyogenes*, *Escherichia coli*, *Streptococci*, *Staphylococci*	Benzylpenicillin
Skin	Interdigital phlegmon	*Fusobacterium necrophorum*, *Dichelobacter* (former *Bacteroides nodosus*)	Benzylpenicillin, Oxytetracycline
	Digital dermatitis	*Treponema* spp.	Oxytetracycline
Eye	Infectious keratoconjunctivitis	*Listeria monocytogenes* *Moraxella* spp mycoplasma	Benzylpenicillin, polymyxin B + oxytetracycline (applied locally)
	Uveitis	*L. monocytogenes*	Polymyxin B + oxytetracycline, benzylpenicillin
Others infections	Systemic infections of newborn ruminants (omphalitis, polyarthritis, meningitis, sepsis)	Several bacterial spp. (*E. coli*, *T. pyogenes*, *Streptococci*, *Staphylococci*)	Trimethoprim, sulfonamides, oxytetracycline, Benzylpenicillin + enrofloxacin
	Umbilical infections	*T. pyogenes*, *streptococci*, *staphylococci*	Benzylpenicillin

Table 4.3 Antimicrobials used for treatment of diseases in cattle and cows.—cont'd

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
	Listeriosis	*L. monocytogenes*	Benzylpenicillin, oxytetracycline
	Tick-borne fever	*Anaplasma phagocytophilum*	Oxytetracycline
	Necrobacillosis	*Fusobacterium necrophorum*	Benzylpenicillin, oxytetracycline (The Finnish Food Safety Authority, 2018; De Briyne et al., 2014a)

antimicrobials to grow poultry (Sahoo et al., 2010; Landers et al., 2012; Boamah et al., 2016). In order to meet the demand, initially scientists began to look for ways to produce more meat at a relatively cheaper level, resulting in the use of antimicrobial agents (Dibner and Richards, 2005). Poultry diseases always involve an entire flock falling ill, which prompts a decision on administration of medicine that must be taken. Several factors affect the decision and the most important of them is the cause behind the disease. Before initiating the treatment, dead or euthanized broilers, chickens, and turkeys, samples of their organs or blood or bacterial samples must be sent for testing to obtain diagnosis. Conducting a field diagnosis is difficult, and antimicrobials are all too often prescribed for precautionary reasons. Phenoxymethyl-penicillin, amoxicillin, and trimethoprim/sulfonamides are mostly used for treating gastrointestinal tract infections, arthritis, and other systemic infections (The Finnish Food Safety Authority, 2018). A summary of the major antimicrobials used in poultry is listed in Table 4.5.

4.3.6 Use of antimicrobials in cats and dogs

The issue of eating dogs and cats is highly emotive, especially in countries like the United Kingdom and United States. In these countries, the idea of consuming a cat or a dog is considered as heinous and amoral, as in United Kingdom and United States cats and dogs are mainly kept as pet animals. Regions where there are records of dog eating include Southeast Asia and Indochina, North and Central America, parts of Africa, and the islands of the Pacific. During the Stone Age and Bronze Age, dog eating was apparently also common in Europe. Still less has been written or discovered about the eating of domestic cats. It has a briefer history than dog eating and the level of consumption of cat meat is also comparatively low. Nowadays, the consumption of dogs and cats still occurs in a number of countries, including China, Thailand, Cambodia, and Vietnam. In 1996, it was proclaimed that dog meat was still being eaten in parts of Eastern Switzerland. It has been estimated that in Asia, around 13–16 million dogs and 4 million cats are eaten each year (Podberscek, 2009). A number of the antimicrobials being used for the treatment of infections in cats and dogs are mentioned in Table 4.6. Commonly used antimicrobials in dogs and cats are beta lactams (particularly cephalexin and amoxicillin-clavulanate in dogs). In dogs, trimethoprim-sulfonamides are the second-most used antimicrobials after beta lactams. In cats, macrolide-lincosamides, azithromycin, and erythromycin are the second-most common class of antimicrobials after beta lactam use for treating skin, ear, eyes, and oral cavity and gastrointestinal tract infections (Wael and Husein, 2011; Nuttall, 2016; Winer et al.,

Table 4.4 Antimicrobials used for treatment of diseases in horse.

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
Skin, subcutaneous tissue	Superficial pyoderma	*Staphylococcus* spp	Aminoglycosides, Enrofioxacin.
	Wounds and abscesses	*Streptococcus* (Vanegas Azuero and Gutiérrez, 2016) *Staphylococcus aureus*	Sulfamethoxazole-trimethoprim, cephalexin, clindamycin, erythromycin (Bowen et al., 2017)
	Cellulitis	*Staphylococcus* and *Streptococcus*	Penicillin-aminoglycoside, trimethoprim-sulfadiazine
	Lymphangitis	*Corynebacterium*, *Pseudo tuberculosis*, *Histoplasma*, *Farciminosum*	Analgesic drugs (morphine) (Fjordbakk et al., 2008), ceftiofur, cefazolin, rifampin, penicillin G, ampicillin, amikacin, enrofloxacin (Wilson, 2001)
Eyes	Corneal ulcers	*Streptococcus equi*, *Zooepidemicus*, *Pseudomonas*, *Aeruginosa*, *Staphylococcus* spp.	Aminoglycosides (solution of gentamycin or tobramycin), Fluoroquinolones (Williams and Pinard, 2013)
Respiratory tract	Sinusitis	*S. equi*, *Streptococcus*, *Zooepidemicus*	Penicillin, TMS, and/or metronidazole (Gordon and Radtke, 2017a)
	Pneumonia	*S. zooepidemicus*, *Rhodococcus equi*, *Klebsiella*, pneumonia.	Erythromycin or azithromycin penicillin G, ceftiofur, TMS, ampicillin-gentamicin
Urinary tract	Cystitis	*E. coli*, *Streptococcus* sp and *Staphylococcus* sp.	Aminoglycosides, gentamicin-penicillin G, or ampicillin (Wilson, 2001)
	Acute Pleuropneumonia	Gram-positive aerobes: (*S. Zooepidemicus*) Gram-negative aerobes	Penicillin G or ampicillin-gentamicin, metronidazole
Mammary gland	Mastitis	*S. zooepidemicus*, *E.coli*, *Klebsiella*, Pneumoniae	Penicillin, gentamicin, amikacin, cephalothin
Urinary tract	Cystitis	*E. coli*, *Streptococcus* sp, and *Staphylococcus* sp.	Aminoglycosides, gentamicin-penicillin G or ampicillin

Table 4.4 Antimicrobials used for treatment of diseases in horse.—cont'd

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
Musculoskeletal system	Septic arthritis	*R. equi*, *Streptococcus*, *Zooepidemicus*	Cefazolin or cephalothin amikacin, gentamicin, oxacillin
	Osteomyelitis	Enterobacteriaceae, *Streptococcus* sp, *Staphylococcus* sp.	Cefazolin or cephalothin amikacin, gentamicin, oxacillin
Oral cavity and gastrointestinal tract	Inflammatory bowel disease (IBD)	Etiology unclear	Dexamethasone, omeprazole (Boshuizen et al., 2018)
	Acute colitis	*Clostridium difficile*, *C. perfringens* (lesser extent)	Acute colitis
	Diarrhea	*Salmonella* sp.	Gentamicin, metronidazole (Wilson, 2001)

2016; Gómez-Poveda and Moreno, 2018). Fluoroquinolones are used commonly in both cats and dogs for treating skin, reproductive tract, and ear infections (Hölsö et al., 2005; Wael and Husein, 2011; Nuttall, 2016; Adel and Khadidja, 2017).

4.3.7 Use of antimicrobials in rabbits

Rabbits are small mammals used as food animals**.** Colibacillosis is a widespread ailment in rabbit's reproduction. It has become one of the chief contagious illnesses that cause danger in the rabbit farming industry (Milon et al., 1999). In commercial farming, the European rabbit (*Oryctolagus cuniculus*), a lactate female can produce a total quantity of milk corresponding to her body mass via four to five pairs of mammae in 35 days (Rosell and de la Fuente, 2018). This attempt predisposes to diseases that affect the mammae throughout lactation. It includes mostly mammary gland microbial diseases like mastitis. In rabbits, diseases by *Pasteurella multocida* are also widespread. Pasteurellosis in them present rhinitis with blood-stained nasal discharge, pneumonia, serous otitis media, pyometra, orchitis, pustule, and septic infection (Langan et al., 2000). Respiratory anthrax is another lethal illness in rabbits in the absence of earlier treatment with antimicrobials. Rabbits are extremely vulnerable to diseases caused by *Bacillus anthracis* spores via intranasal instillation; they succumb within 2–4 days post illness. For the prevention and cure of diseases, different antimicrobials including penicillin, ampicillin, linezolid, chloramphenicol, rifampin, vancomycin, ciprofloxacin, levofloxacin, moxifloxacin, doxycycline, amoxicillin, clindamycin, and meropenem are used (Li et al., 2013). Antimicrobials used for rabbits are listed in Table 4.7.

4.4 Aquaculture

Aquaculture includes all forms of culturing aquatic animals and plants in marine, fresh, and brackish environments (Pillay and Kutty, 2005). Aquaculture is one of the most hopeful alternatives for

Table 4.5 Antimicrobials used for treatment of diseases in poultry.

Therapeutic area	Disease	Causative microbe	Antimicrobial use
Gastrointestinal tract	Necrotic enteritis	*Clostridium perfringens*	Phenoxymethyl-penicillin* amoxicillin*, tylosin, trimethoprim-sulfonamides, tetracycline
Musculoskeletal system	Tenosynovitis in broiler breeders	*Staphylococcus aureus*	Phenoxymethyl-penicillin* amoxicillin*, trimethoprim
	Arthritis (in turkeys)	*S. aureus*	Phenoxymethyl-penicillin*, amoxicillin*, trimethoprim-sulfonamides, tetracycline
Other infections	Erysipelas	*Erysipelothrix rhusiopathiae*	Phenoxymethyl-penicillin*, amoxicillin*, trimethoprim-sulfonamides, tetracycline
	Pasteurella infection (in adult chickens and turkeys)	*Pasteurella multocida*	Phenoxymethyl-penicillin*, amoxicillin*, trimethoprim-sulfonamides, tetracycline
	Colibacillosis (a systemic infection)	*Escherichia coli*	Amoxicillin*, tetracycline (De Bryne et al., 2014a; The Finnish Food Safety Authority, 2018)

proficiently and sustainably increasing the production of animal proteins (Liao and Chao, 2009). To meet the protein demands of growing global populace, aquaculture is considered to be the fastest protein food production sector and accounts for 50% of overall food supply (Okocha et al., 2018). Aquaculture include fishes, catfish , Atlantic salmon, rainbow trout, tilapia, Pacific oyster, Eastern oyster, Pacific white shrimp, yellow perch, and bluegill sunfish, mollusks, etc. Nowadays, freshwater pool aquaculture farming major product is finfish. For freshwater farming, diverse sources of water supply like containers, pools, streams, and channels are used. Aquaculture farming generally consists of cage culture for sea finfish and freshwater pools or brackish water for crustaceans (Hall, 2011). Whilst many cages and pools benefit from natural water exchange used for provision of oxygen and waste disposal, simultaneously the fish and crustaceans are exposed to illness-causing microbes present in the water. To improve aquaculture farming, new techniques have been developed including closed recirculating aquaculture systems that decrease the risk of disease vectors and wastes (Martins et al., 2010).

Table 4.6 Antimicrobials used for treatment of diseases in cats and dogs.

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
Skin	Lesion and superficial skin inflammation	*Staphylococcus pseudintermedius*	Fluoroquinolones
	Superficial skin infection (hair follicle infection, impetigo)	*Staphylococcus intermedius*	Amoxicillin, clavulinic acid, cefotraxione, ciprofloxacin (Wael and Husein, 2011)
	Deep skin infection (canine pyoderma)	*Staphylococcus intermedius*	Clavulanate, amoxicillin, lincomycin, clindamycin, cefovecin, cefpodoxime, marbofloxacin, difloxacin, orbifloxacin, enrofloxacin, azithromycin, tobramycin, pradofloxacin, rifampin, amikacin, netilmicin, chloramphenicol, gentamicin (Ferran et al., 2016)
	Wounds and abscess	*Pasteurella multocida*, *Staphylococcus* spp., obligate anaerobes	Amoxicillin, cephalosporins, Fluoroquinolones, metronidazole, clavulunate (Roy et al., 2007; Little and Kennedy, 2010)
Ear	Otitis externa	*Staphylococcus*, *Malassezia*, *Pseudomonas*	Polymixin B, fusidic acid, florfenicol, gentamicin, enrofloxacin, neomycin marbofloxacin, cefadroxil, amoxicillin, miconazole, clindamycin, lincomycin, fluoroquinolones (Nuttall, 2016)
Respiratory tract and thoracic cavity	Pneumonia	*Streptococcus canis*, *Mycoplasma* spp., Chlamydia felis, *Bronchiseptica*, *Zooepidemicus*, *Bordetella*	Doxycycline, fluoroquinolone' penicillin, clindamycin ampicillin-sulbactam
	Bronchitis		

Continued

Table 4.6 Antimicrobials used for treatment of diseases in cats and dogs.—cont'd

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
		Chlamydophila spp., *Escherichia coli*, *Mycoplasma* spp., *streptococcus* spp, *Bronchiseptica*, *Bordetella*	Doxycycline, amoxicillin, clavulanate, amikacin
	Pyothorax	*Fusobacterium*, *Prevotella*, *Clostridium*, *Bacteroides*, *Peptostreptococcus*, *Streptococcus* spp., *Mycoplasma* spp. *Porphyromonas*, *Pasteurella* spp, *actinomyces*	Enrofloxacin, marbofloxacin, penicillin clindamycin(Lappin et al., 2017)
Oral cavity and gastrointestinal tract	Gingivitis, periodontitis	*Streptococcus*, *staphylococcus*, *Enterococcus*, *actinomyces* sp., *lactobacillus* sp. (mostly in dogs) (Pieri et al., 2012)	Tetracyclines, clindamycin amoxicillin, clavulanate metronidazole (Hale and FAVD)
	Root abscess	*Pasteurella*, anaerobes	Chloramphenicol, azithromycin, metronidazole, amoxicillin, (Winer et al., 2016)
	Inflammatory bowel disease	*Campylobacter jejuni*, *Clostridium difficile*, *Clostridium perfringens*, *Salmonella* (Honneffer et al., 2014)	Tylosin, oxytetracycline, metronidazole (Simpson and Jergens, 2011)
	Anal sac inflammation	Gram-positive cocci, gram-negative cocci, gram-positive rods, gram-negative rods (Frankel et al., 2008)	Cefovecin, enrofloxacin, orbifloxacin
	Diarrhea	*Enterobacteriaceae*, *streptococcus* Gamma-, beta-Proteobacteria, *Bacilli*, *Collinsella*, *Clostridium* (Suchodolski et al., 2015)	Metronidazole (De Briyne et al., 2014a)

Table 4.6 Antimicrobials used for treatment of diseases in cats and dogs.—cont'd

Therapeutic areas	Diseases	Causative microbes	Antimicrobial use
Reproductive tract	Prostatitis	*Staphylococcus* spp., *Klebsiella* spp., *E. coli*, *Pseudomonas* spp., *Pasteurella* spp., *Mycoplasma* spp., *Ureaplasma* spp. (Niżański et al., 2014)	Tetracycline fluoroquinolone, sulfamethoxazole, chloramphenicol, trimethoprim (Sykes, 2013; Adel and Khadidja, 2017)
	Pyometra	*E. coli*	Sulfadoxine, amoxicillin, trimethoprim, clavulanic acid (Fieni et al., 2014)
Urinary tract	Urinary tract infections (UTIs)	*E. coli* (52.5%), *Staphylococcus* spp., *Enterococcus* spp.	Amoxicillin, cephalexin, sulfamethoxazole, clavulanic acid, enrofloxacin (Wong et al., 2015)
Musculoskeletal system	Arthritis	*Staphylococcus aureus*, *staphylococcus* spp. *Pseudomonas aeruginosa* (Marchandeau et al., 2014)	Amoxicillin-clavulanic acid, cephalosporin, clindamycin, enrofloxacin amikacin, azathioprim (Soontornvipart et al., 2003)
Eyes	Conjunctivitis	*Enterococcus* spp., *Micrococcus* spp., *Pseudomonas* spp. *Pasteurella* spp., *staphylococci*, *Mycoplasma*, *Bacillus* spp., (Płoneczka-Janeczko et al., 2017)	Penicillins, fusidic acid, cephalosporins, aminoglycosides, oxytetracycline, polymyxin, erythromycin (Gómez-Poveda and Moreno, 2018)
	Melting keratitis	*Pseudomonas aeruginosa*, Staphylococcus and Streptococcus spp.	Atropine, cyprofloxacincollyre, hyaluronic acid, NAC 10% (Ion et al., 2015)
Other	Leptospirosis	*Leptospira* (Miotto et al., 2018)	Penicillins, doxycycline
	Lyme borreliosis	*Borrelia* spp.	minocycline, amoxicillin clarithromycin, ceftriaxone, erythromycin, cefotaxime, doxycycline (Littman et al., 2018)

Table 4.7 Antimicrobials used for treatment of diseases in rabbits.

Therapeutic area	Disease	Causative microbe	Antimicrobial use
Respiratory tract	Pasteurellosis	*Pasteurella multocida* (*coccobacillus*)	Enrofloxacin, (1–3), (1–6) β-glucans (Palócz et al., 2014)
Gastrointestinal tract	Epizootic Rabbit Enteropathy	*Escherichia coli*, *Haemophilus paracuniculus* , *Proteus mirabilis*, *Citrobacter* spp. and *Klebsiella* spp.	Lincomycin, spectinomycin and neomycin, tylosin, apramycin, bacitracin, tiamulin (Puón-Peláez et al., 2018)
	Diarrhea	*E. coli*, *Eimeria* spp., adenovirus, coronavirus, *salmonella* spp., *Yersinia* spp.	Sulfonamides, tetracyclines, and neomycin (Banerjee et al., 1987)
	Intestinal Coccidiosis	*Eimeria* spp.	Prophylactic (bifuran, sulfa drugs, amprosol) (Bhat et al., 2010)
Eyes	Myxomatosis	*Myxoma* virus	Vaccination (Marchandeau et al., 2014)
	Phacoclastic uveitis	*Encephalitozoon cuniculi*	Surgery (phacoemulsification) (enucleation) (Sandmeyer et al., 2011)
Skin and Musculoskeletal system	Pododermatitis	*Pasteurella* sp. or *Staphylococcus aureus.*	Antiseptic products: salicylic acid mupirocin, neomycin
	Abscesses	*Pasteurella* sp. or *S. aureus*	Cephalosporin or azithromycin (Esther van Praag)
Ear	Otitis media/interna	*Pasteurella multocida*, *Streptococcus* spp., *E. coli*, *Enterococcus* spp., *Pseudomonas* spp.	Chloramphenicol and penicillin, ciprofloxacin, enrofloxacin-marbofloxacin-penicillin chloramphenicol

4.5 Global aquaculture trends

Worldwide aquaculture has developed significantly over the past 50 years to around 52.5 million tons (68.3 million, counting sea-going plants), in 2008 worth US$98.5 billion (US$106 billion, counting oceanic plants) and contributing to around 50% of the world's aquatic food supply. Asia dominates this production, accounting for 89% by capacity and 79% by cost; among Asian countries, China is the leading producer (32.7 million tons in 2008). The speedy development in this region is due to different factors that include preexisting aquaculture practices, populace and financial development, relaxed regulatory framework, and expanding export opportunities. Countries contributing more in aquaculture than wild-caught fish are China, India, Vietnam, Bangladesh, and Egypt. The top 15 aquatic culture—producing countries in 2010 by percentage of total worldwide production appear in Fig. 4. 2. It has been reported that China is contributing more than 60% of the worldwide aquaculture production and also using bulk antimicrobials to guarantee sufficient production and disease management. During the 1980s—1990s, development in aquaculture was rapid in Europe and North America, but since this time it has stagnated, probably owing to administrative restrictions on sites and other competitive factors, though they have continued the growth of markets for fish and seafood (Bostock et al., 2010).

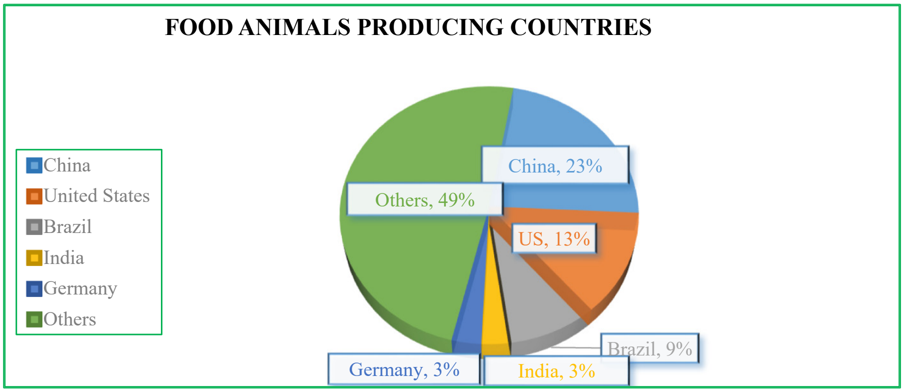

FIGURE 4.1

Top five countries and percentages of their shares in global antimicrobial consumption in food animals in 2010 (Van Boeckel, Brower et al., 2015).

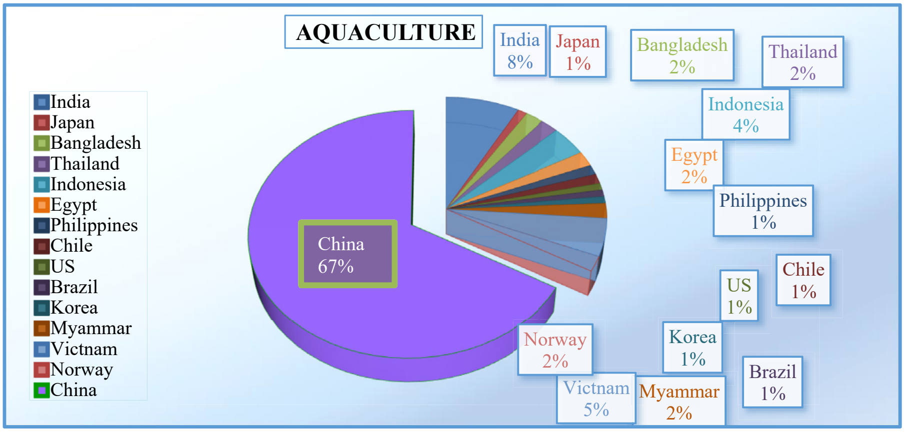

FIGURE 4.2

Top 15 aquatic culture—producing countries in 2010 by percentage of total worldwide production (FAOSTAT., Accessed Nov 24, 2014. http://www.faostat.fao.org.)

By 2015 we outreached to a point where the marine food consumed worldwide was ~160 million metric tons, Mmt and was grown in farms rather than taken from natural sources. This 80 Mmt of farmed marine food consisted of fish, shellfish, shrimps, and seaweed, with approximately 90% farmed in Asia. By 2050, it is expected that worldwide aquaculture production will double, with well-managed fisheries predicted to demise over this time period. Undoubtedly, aquaculture will be a major contributor to the protein supply for the future overall diet (Stentiford, February 2, 2017). Fig. 4.3 indicates aquatic culture expanding to meet world fish demand.

4.6 Need for aquaculture

In the last 60 years, swine, poultry, and cattle production has increased globally while the poultry production surpassed the others. Around 1985, aquaculture was the only animal producing industry globally. Prior to this era, aquaculture was considered as a noncommercial matter, a traditional way of life and a source of nourishment for its producers. Increased demand for a healthy choice of protein, enriched seafood feed production, reduction of numbers of wild fish, and advanced farming techniques have led to high-density fish production in recent years (Cole et al., 2009). Up to 80% reduction in global finfish and shellfish stocks (collectively as "fish") occur in order to provide food to increasing

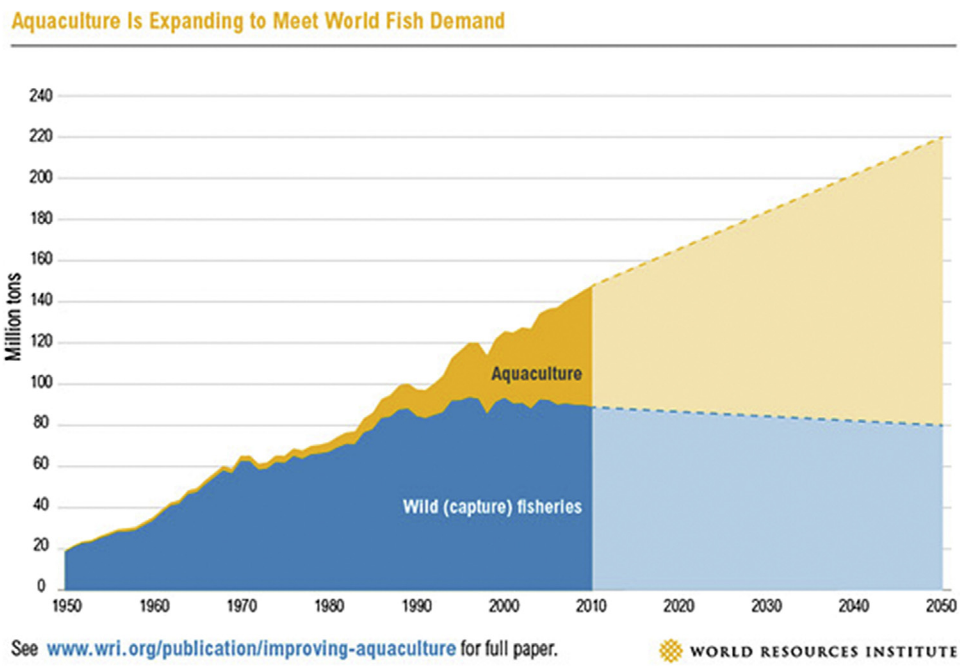

FIGURE 4.3

Aquatic culture expanding to meet world fish demand.

Adapted from (Waite, R. June 2014. Aquaculture Is Expanding to Meet World Fish Demand. *World Resources Institute: https://www.wri.org/resources/charts-graphs/aquaculture-expanding-meet-world-fish-demand).*

human population day by day (Pauly and Zeller, 2016, 2017). Due to its capability to provide sensible, secure, reliable, and alternative food producing systems, our dependency on aquaculture has increased to reduce this extinction. Aquaculture systems produced 70.5 million tons of food fish and 26.1 million tons of aquatic algae in 2014. According to aquaculture production figures, a significant contribution of aquaculture resulted in increasing the total fish consumption from 1962 to 2002 from 5% to 49%, respectively. It is predicted that the production of aquaculture in Europe will reach 4 million tons by 2030 (Pauly and Zeller, 2017). This globally increased production of aquaculture has resulted in new and improved farmed spp., more than 580 species in total (consisting of 362 finfish and 62 crustaceans), with a wide range of growth and maximum production conditions (Pauly and Zeller, 2017; Naylor et al., 2000).

4.7 Legislation concerning antimicrobial use in aquaculture

Antimicrobial usage in aquaculture farming is governed by a range of factors that include laws and policies by the particular management union, the unique microbes that exist and their antimicrobial sensitivities, the medication period, the illness condition of the host, and the system framework, like saltiness, temperature, light phase, etc. Statistics related to the antimicrobial dosages used in aquaculture are limited, as only some countries scrutinize the amount of antimicrobials used (Sapkota et al., 2008). Specifically in Europe, North America, and Japan, policies regarding antimicrobial consumption are stringent and fewer antimicrobials are approved for use in aquaculture farming. In 2001, the European Veterinary Medicinal Products Directive, as amended and codified in Directive (2001)/82/EC, excluded the prophylactic usage of antimicrobials for aquaculture (Committee, 2004; Watts et al., 2017). In spite of productivity rate >20-fold, Norway instituted strict regulations for antimicrobial usage, with 99% decrease between 1987 and 2013 in combination with improved vaccinations; their outstanding stewardship has been certified (Watts et al., 2017).

4.8 Antimicrobial agents used in aquaculture

Aquaculture leads to the endorsement of conditions that facilitate spreading the number of illnesses and harms. A broad variety of compounds are used in aquaculture farming that include antimicrobials, pesticides, hormones, anesthetics, a variety of pigments, mineral deposits and vitamins, though not all of them are antimicrobials. As with livestock animal production, antimicrobials are also used in aquaculture in attempting to cure ailments (Burka et al., 1997). Antimicrobial treatment patterns also differ among countries and among individual aquaculture farming within the same country. The most important reason to follow antimicrobial usage is to control contagious illnesses in breeding areas, to avert losses in farming; to limit the introduction of microbes to new facilities when larvae, fry, or brood stock are moved; to limit the disease spreading to natural fish via the reproduction sewage or when cultured fish are stocked out; and to avoid the strengthening of microbes previously widespread in a watershed (Phillips et al., 2004). There are inadequate statistics concerning antimicrobial usage in global aquaculture. For many of the farmed genuses, we are deficient in sufficient information regarding pharmacokinetics (Sapkota et al.) and pharmacodynamics of drug administration. The drugs available for the cure of widespread transmittable illnesses are becoming increasingly inadequate and costly and, in several situations, not available due to the emergence of drug resistance that is shocking and erases the previous 60 years' medicinal developments (Serrano, 2005). In aquaculture farming antimicrobials have been used predominantly for curative purposes and as prophylactic agents (Serrano, 2005; Shao, 2001). Drugs are rarely used as growth promoters in aquaculture farming. Prophylactic treatments when used are typically confined for breeding, the immature or larval stages of aquatic animal farming. Prophylactic usage is more typically found in lower-level farming units that can't afford or get access to the recommendation of veterinary professionals.

4.9 Route of antimicrobial usage in aquaculture

In the marine environment antimicrobials are typically used during the fatten phase. Antimicrobials in aquaculture farming are delivered via feed medication, bioencapsulation, immersion baths, dip, flush, or in exceptional cases, intramuscularly or intraperitoneally (Smith et al., 2008). Feed medication is not completely digested by fish, and most of the time is inadequately digested and metabolized, with the result being that there is a continuous release of antimicrobials into the surroundings. Medicated feed also primarily affects the gut flora of fish (Navarrete et al., 2008). Consistent presentation to antimicrobials leads to the variety of resistant microbes and an increase in antimicrobial-resistant genes (ARGs) transfer. These circumstances eventually imply that the feces of feed-medicated fish are affluent in ARGs (Martinez and Baquero, 2000).

4.10 WHO list of antimicrobials used in aquaculture

The World Health Organization (WHO) catalog is a classification of 260 antimicrobials. The catalog was proposed as a reference for the people and veterinary health establishment to prioritize threat measurement with respect to increase in antimicrobial resistance. Two criteria are measured for incorporation in the catalog: first, for the treatment of genuine human illnesses the antimicrobial should be the only way or one of the few accessible therapies and, second, it ought to be used to treat illnesses caused either by microbes that might be transferred to human via nonhuman origin (Magouras et al., 2017) or human illnesses caused by microbes that could gain resistant genes from nonhuman origin. "Crucially significant" antimicrobials met both criteria. "Most significant" antimicrobials met any one of the criteria, and "significant" antimicrobials are those that do not meet any criterion but still are considered important antimicrobials. The WHO catalog included six widespread classes of antibiotics like aminoglycosides, macrolides, penicillins, quinolones, sulfonamides, and tetracyclines and are frequently used in aquaculture farming and cultivation.

4.11 Unregulated use of antimicrobials in aquaculture

Unregulated use of antimicrobials in aquaculture industry might cause individual well-being and foodstuff security concern. A result of the utilization of the antimicrobials in food animals is the occurrence of medicine residues, even in a smaller amount, in the eatable tissues of the treated creature. Antimicrobials used in accordance to brand instructions must not result in residues at butchery. The explanation for residues occurrence in eatable tissues of animals suggests multiple reasons; noncompliance of prescribed extraction period; dispersion of excess quantity of drug at a particular inoculation site; utilization of antimicrobial-polluted tools, or failure to appropriate hygienic apparatus used for mixing or managing medicines; assimilation error; inadvertent feed with chemical spill or feed medication; animal characteristics like age, pregnancy, inborn ailment, and hypersensitivities; chemical reactions among medicines; changes in heat for water spp.; ecological pollution; and inappropriate drugs usage (Okocha et al., 2018).

Drug residues in aquaculture foodstuffs can result in resistant bacterial growth and be poisonous to customers, which can lead to morbid conditions or death. For example, chloramphenicol residues increase the possibility of cancer and in lower concentration may produce aplastic anemia; other lethal effects include hypersensitivity by penicillin, mutagenicity and nephropathy by gentamicin, and immunopathology and carcinogenic effects by sulfamethazine, oxytetracycline, and furazolidone (Beyene, 2016).

4.12 Use of antimicrobials in fish

Fish as foodstuff contribute about 17% of overall animal proteins; out of this, half originate from aquaculture farming (Troell et al., 2014). The aquaculture farmed fish spp. included salmon, turbot, marine bass, marine bream, trout, tuna, sole, halibut, cod, and European eel. In Ireland, Norway, and Scotland, marine enclosed aquaculture farming is mainly restricted to salmon, and marine bass and marine bream in Italy, Greece, and Spain. Recently, a rise in the tilapia and mullet farming have been observed in Egypt. The salmon production in Chile is continually affected by microbes such as bacteria, parasites, fungi, and viruses responsible for progression of illnesses, numerous of which resulted in the loss of millions of finfish and thus major farming loss (Asche et al., 2009). Over the last 30 years, the facultative intracellular bacterium *Piscirickettsia salmonis*, causative agent of Salmonid Rickettsial Syndrome (SRS) consistently overwhelmed the salmon farming (Rozas and Enriquez, 2014). The bacterium is responsible for >80% of finfish deaths that happened due to contagious illnesses in the three chief fish group cultured in Chilean industry, i.e., *Salmo salar* (Atlantic salmon), *Oncorhynchus kisutch* (coho salmon), and *O. mykiss* (rainbow trout) (Makrinos and Bowden, 2017). Between 2007 and 17, salmon farming industry utilized >5500 tons of antimicrobials with each ton of salmon production receiving a standard of 500 g antimicrobials in accordance to a statement by the national fisheries service (Sernapesca). The two broad-spectrum antibiotics frequently administered in salmon farming are florfenicol and oxytetracycline. In 2017, 393.9 tons of antibiotics were used, among them 92.2% of florfenicol, 6.7% of oxytetracycline, and the remaining 1% correspond to erythromycin and amoxicillin (Lozano et al., 2018). The antimicrobials used for fishes appear in Table 4.8.

4.13 Use of antimicrobials in crustaceans

Crustaceans have been an essential diet source for people for many years. Almost all crustacean diseases have viral etiology except two or three. For the cure of such diseases, there are no well-known antimicrobials. The alternatives available include devastation or separation of tainted stocks and amendment of on-farm husbandry measures. Due to the unavailability of antiviral drugs for shrimp diseases, a few defensive procedures are brood stock screening programs and decontamination of farmed tools or pool services. The few antimicrobials and preventive measures adopted for crustaceans are presented in Table 4.9. Hence, in few circumstances excess of chloride and lime might be the single solution for infected stock devastation and pool disinfection purposes. For the earlier identification of

Table 4.8 Antimicrobials use for treatment of diseases in fishes.

Affected spp.	Diseases	Causative microbes	Antimicrobial use
Fin fish	Tenacibaculosis	*Tenacibaculum maritimum*	Oral broad-spectrum antibacterials
Fin fish	Vibriosis	*Vibrio anguillarum*, *Vibrio ordalii*	Caprylic acid with broad-spectrum antibacterials
Fin fish	Epitheliocystis	*Chlamydia* spp.	Broad-spectrum antibacterials
Fin fish	Botulism	*Clostridium botulinum*, *Clostridium argentinense*, *Clostridium butyricum*	Guanidine hydrochloride (spickler, July 2007: http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php #46)
Salmonid	Bacterial gill disease (BGD)	*Flavobacterium branchiophila*	Florfenicol, oxytetracycline, chloramine T
Salmonid	Piscirickettsiosis	*Piscirickettsia salmonis*	Broad-spectrum antibacterials
Salmonid	Furunculosis	*Aeromonas salmonicida*	Sulfadiazine, trimethoprim, old quinolones (1st and 2nd generations) oxolinic acid, flumequine (Sekkin and Kum, 2011)
Salmonid	Infectious salmon anemia (ISA)	Isa virus	Virus inactivated by disinfectants (chloramine-T, iodophors, Virkon S) (spickler, March 2010 : http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php #36)
Salmonid	Infectious hematopoietic necrosis(IHN)	Rhabdoviridae	Virus inactivated by disinfectants (Spickler, July 2007 : http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php #45)
Rainbow trout	Rainbow trout-Gastro Enteritis (RTGE)	*Candidatus arthromitis*	Broad-spectrum antibacterials
Rainbow trout, salmonids, Catfish	Enteric red mouth disease (ERM)	*Yersinia ruckeri*	Sulfadiazine, trimethoprim, old quinolones
Rainbow trout, Redfin perch	Epizootic hematopoietic necrosis (EHN)	*Iridoviridae ranavirus*	Virus inactivated by disinfectants (Spickler,

Table 4.8 Antimicrobials use for treatment of diseases in fishes.—cont'd

Affected spp.	Diseases	Causative microbes	Antimicrobial use
			July 2007 : http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php #46)
Trout	Red mark syndrome	*Flavobacterium psychrophilum*	Broad-spectrum antibacterials (Sekkin and Kum, 2011)
Trout	Viral hemorrhagic septicemia	*Novi rhabdovirus*	Antivirals (spickler, March 2010: http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php #36)
Turbot	Furunculosis	*Aeromonas salmonicida*	Sulfamerazine (Snieszko, 1954)
Catfish	Hemorrhagic septicemia	*Aeromonas veronii*	Amoxicillin, gentamicin, ofloxacin (Deemagarn and Tohmee, 2014)

Table 4.9 Antimicrobials used for treatment of diseases in crustaceans.

Affected spp.	Disease	Causative microbe	Antimicrobial use
Crustacean	Vibriosis	*Luminous Vibrio* spp. (*V. harveyi*)	Oxytetracycline, quinolones
Crustacean	Necrotizing hepatopancreatitis (NHP)	Intracellular proteobacteria	Oxytetracycline
Crustacean	Gaffkaemia	*Aerococcus viridans*	Oxytetracycline
Prawns	Vibrio infections	*Vibrio Parahaemolyticus*	Oxytetracycline
Prawns	Bacterial shell disease	*Vibrio anguillarium*, *Pseudomonas* spp., *aeromonas* spp., *Vibrio* spp.,	Oxytetracycline
Shrimp	Vibrio infections	*V. Parahaemolyticus*	Oxytetracycline, furazolidine, prefuran
Shrimp	Bacterial shell disease	*V. anguillarium*, *aeromonas* spp.,	Prefuran, oxytetracycline
Shrimp	Protozoan infections	*Zoothammium* spp.	Prefuran
Shrimp	Larval mycosis	*Lagenidium* spp.	Treflan (Alderman et al., 1998)

necrotizing hepatopancreatitis caused by *Vibrio* spp., shrimps are treated with oxytetracycline via medication feed. *Vibrio* spp. show resistance to antibiotics like chloramphenicol, furazolidone, oxytetracycline, and streptomycin (Rodgers and Furones, 2009).

4.14 Use of antimicrobials in mollusks

Mollusks like snails, oysters, and bivalves are also a food source for humans. Mollusks as a foodstuff may also contribute to the prevention of diseases by providing key nutrients, immunostimulatory compounds, and other secondary metabolites (Benkendorff, 2010). Mostly mollusks are affected by viral or parasitic diseases and it is not feasible to exploit any antimicrobial in open seawater culturing. The mollusk parasitic illnesses are often intracellular (e.g., *Bonamia ostreae*) and no antimicrobials are available for cure. It might be probable to monitor behavioral changes in several stocks, especially brood stock and larvae in hatcheries, and collection of complete evidence (e.g., aquaculture features like hotness and salinity etc.) may also be useful for manipulation of restricted surrounding conditions. This is in fact possible in a controlled hatchery situation, where infections can break out very rapidly in vulnerable stock. Larvae stage feed behaviors may also present an earlier sign of health troubles. Indication of weakness includes gaping shells in immature or adult stages, which can also be used to forecast possible harms, as diminished growth in motile genuses, e.g., scallops, clams. However, particular substitutes are needed for mollusks. These usually include reduction in stock mass, changes in saltiness, and lower water temperature, as well as avoidance of the transfer of shellfish from known enzootic areas (Rodgers and Furones, 2009). Preventive measures adopted for mollusks are presented in Table 4.10.

4.15 Future perspectives

Demand for animal protein by humans is rising globally at an uncontrollable rate, which leads to wide usage of antimicrobials at greater extent for disease prevention and growth promotion in food animals. Patterns of antimicrobial consumption in middle-income and high-income countries differ in many respects. Mapping the antimicrobial consumption in livestock provides a baseline estimate of its global importance. Low-income countries lack in knowledge based on consumption of antimicrobials results to intense AMR in food animals. Globally, intensive livestock farming has increased food production at a low cost per unit produced, but at an unrecognized price paid in increased antimicrobial resistance (Van Boeckel et al., 2015).

The unique advantages of antimicrobials use in food animals are definite targeting of pathogens, well-known mechanisms of activity, and preferable stability for administration, for the prevention and treatment of bacterial and parasitic diseases, for the improvement of animal food production, and protection of the environment and public health. Absence of antimicrobials use in food-producing animals may cause deleterious effects on production of food derived from animals and, thus, on public health. Contrary to that, it is also important to administer antimicrobials to animals in ways that avoid the negative impacts. In the near future, it is expected that no new class of antimicrobials is going to be administered in food animals. Keeping in view the development of antimicrobial resistance in food animals, our aim is to act against AMR by taking preventive measures such as vaccination, advanced farm management, implementation of improved farming systems, upgraded techniques used for better hygiene on farms, and cautious and sagacious use of antimicrobial agents.

Table 4.10 Preventive measures adopted for mollusks.

Affected spp.	Diseases	Causative microbes	Treatment/Control
Oyster	Iridovirosis (oyster velar virus disease)	Iridoviridae	No treatment, brood stock screening, stock destruction and pond disinfection
Oyster	Herpesvirosis (oyster Herpes-like virus disease)	Herpesviridae	No treatment or control
Oyster	Bonamiosis	*Bonamia ostreae*, *Bonamia* sp.	No treatment, reduced stocking densities, lower water temperature
Oyster	Perkinsosis	*Perkinsus marinus*, *Perkinsus olseni*, *Perkinsus* spp,	No treatment, development of resistant oyster stocks (Rodgers and Furones, 2009)
Oyster	Roseovarius oyster disease	*Roseovarius crassostreae*	No treatment, selective breeding of oysters
Oyster	Haplosporidiosis	*Haplosporidium costale*, *Haplosporidium nelsoni*	No treatment, sterilization and filtration of inflow water (Rodgers and Furones, 2009)
Mollusks	QX disease (Marteiliosis)v	*Marteiliare fringens*, *Marteilia maurini*, *Marteilia sydneyi*,	No treatment. high salinity (Maloy et al., 2007; Zannella et al., 2017)
Mollusks	Brown ring disease *Tapes philippinarum*	*Vibrio tapetis*	Nitrofurans (Rodgers and Furones, 2009)
Mollusks	Pacific oyster nocardiosis	*Nocardiacrass ostreae*	No treatment, sterilization and filtration of inflow water (Zannella et al., 2017)

Therefore, more research is required to understand how antimicrobials are being used and how to cope with their inappropriate uses in nature (Hao et al., 2014). Moreover, research must also be done to identify the resistance-causing genes in microbes and food animals. Identification of mobile genetic elements and modes of spreading of these elements would needs also to be investigated and researched. Raising livestock without using antimicrobial agents is impossible, therefore, qualitative and quantitative analysis of antimicrobials must be done. More advanced dosage schemes can help brighten the future of antimicrobial trends in food animals (Hao et al., 2014).

4.16 Conclusion

With extensive animal production, microbial and pathogenic diseases became more chronic, caused by *Actinobacillus pleuropneumoniae*, *E. coli*, *Clostridium welchii*, *S. aureus*, *S. pneumonia*, *Salmonella*, and others. More than a hundred antimicrobials, including β-lactams, aminoglycosides, tetracyclines, amphenicols, macrolides, sulfonamides, fluoroquinolones, lincosamides, polypeptides, and polyene, have been used for the production of food for animals and aquaculture throughout the world. These antimicrobials have played a crucial role in prevention, treatment, and control of animal diseases caused by microorganisms. Due to certain advantages, such as exact targeting of pathogens, well-known mechanisms of activity and desired stability, antimicrobials have justified their usage in food animals and aquaculture, thus playing a main part in the prevention and treatment of bacterial and parasitic diseases. The improper use of antimicrobials is the main cause of development of antimicrobial resistance. As a result of AMR in food animals and aquaculture, costs/charges to treat antimicrobial-resistant infections in humans have also increased. It is well acknowledged that the problems relating to antimicrobial use in animal food and aquaculture are of global concern. But still, pharmacological research on food animals and aquaculture drugs has helped to lessen the possibility of noxious resistance and sporadic public health and environmental concern. As well, advanced and more productive medicines are required for future successful animal production.

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