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Antibiotic Classes and Antibiotic Susceptibility of Bacterial Isolates from Selected Poultry; A Mini Review

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ABSTRACT
Antibiotics are drugs that kill (bactericidal) or slow (bacteriostatic) the growth of bacteria. Broad-spectrum antibiotics treat a wide range of infections, while narrow- spectrum antibiotics are effective against only a few types of bacteria. Antibiotics are very essential in the treatment of human and animal infections caused by bacteria. They are also important for the prevention of secondary infections. Despite the importance of antibiotics, their uses have received much criticism from the consumers, responsible stakeholders and policy makers. Antibiotics have evolved over the years with relatively unprecedented resistant patterns. Various classes of antibiotics such as aminoglycosides, cephalosporins, macrolides, quinolones, tetracyclines and many more have also evolved. For instance cephalosporins have evolved from first generation to the fifth generation. These antibiotic groups use different mechanisms in combating bacteria. These mechanisms include disrupting the formation of bacteria cell wall (penicillins, cephalosporins), interfering with the synthesis of bacteria DNA (fluoroquinolones), inhibiting the bacterial protein synthesis (tetracycline) and destroying protein synthesis (macrolides, aminoglycosides). Bacterial isolates from poultry exhibit different resistance patterns. At times the resistance patterns may be the same or similar among bacterial isolates. The differences in resistance patterns are widely due to factors which include differences in geographical locations, particular bacteria species involved, the animal production systems, the extent to which antibiotics are used, sampling techniques and period of sampling.

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INTRODUCTION

The prevalence of antibiotic resistance pathogens in poultry and other farm animal species is a concern worldwide and has caught the attention of researchers, health organizations, governments and all stakeholders (Adzitey, 2011). Such data gives an idea of the possibility of resistant genes and pathogenic organisms being transferred from poultry to other farm animals and/or humans. Studies for determining the antibiotic susceptibility of bacteria isolates including that of poultry have relied mainly on the disk diffusion method, in addition to the agar and broth dilution methods (Stalons et al., 1975 and Bauer et al., 1966). The agar most frequently use is the Mueller-Hinton agar (Nobile et al., 2013; Adeleke and Omafuvbe, 2011; Kilonzo-Nthenge et al., 2008 and Cormican et al., 2001). Recent advances have been made through the use of modern procedures and technologies at the molecular level to identify and to isolate resistant genes (Adzitey et al., 2013a and Faldynova et al., 2013).

Campylobacters, *Escherichia coli*, *Salmonellae*, *Listeria*, *Klebsiella*, *Enterobacter* and *Pseudomonas* species are among the bacteria that have been isolated from poultry and have exhibited different resistant patterns to antibiotics (Adzitey et al., 2015; Geck et al., 2013; Alvarez-Fernandez et al., 2013; Adzitey et al., 2012a and Adzitey et al., 2011). Antibiotics continue to play very important role in decreasing diseases, illness and/or death associated with bacterial infections in poultry, other farm animals and humans. Nonetheless the use of antibiotics as growth promoters and therapeutic purposes have been the major driving force behind the emergence and spread of drug-resistance bacteria among pathogenic and non-pathogenic bacteria strains (Adzitey et al., 2013b; Adzitey et al., 2012b; Adzitey et al., 2012c and Aarestrup et al., 2008).

The mini review gives examples of the antibiotic susceptibility of bacteria isolated from poultry and the classes/mechanisms of some antibiotics.

Antibiotic susceptibility of poultry bacterial isolates

Poultry meat is important in the diet of many people worldwide. It is among the meat types with little objection as afar as religious beliefs are concern. Continues increase in world's population and better acceptability of poultry meat worldwide suggest that, demand for poultry meat will continue to increase. This will also put pressure on the poultry industry to increase meat supply. Strategies that will be put in place to achieve increase supply of poultry meat will

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include the use of efficient breeds, appropriate balance diets, the use of growth promoters and many more. Currently, many antibiotics are used in the poultry industry either as growth promoters or for prevention, control and treatment purposes. For instance bacitracin, chlortetracycline, erythromycin and penicillin are used in poultry production for prevention and treatment of diseases (Kilonzo-Nthenge et al., 2008). Antibiotics including bambermycin, avilamycin and efrotomycin are used as growth promoters (Butaye et al., 2003). Numerous researches have been conducted on the antibiotic susceptibility of poultry bacterial isolates. In this mini review, only few examples have been given.

Campylobacter jejuni strains isolated from ducks were resistant to cephalothin (99%), suphamethoxazole/trimethoprim (96%), tetracycline (96%), nalidixic acid (84%), ampicillin (81%) and norfloxacin (80%), but susceptible to gentamicin (95%), chloramphenicol (89%) and erythromycin (88%) (Adzitey et al., 2012b). All *C. coli* duck isolates were resistant to cephalothin, nalidixic acid, norfloxacin and tetracycline but susceptible to chloramphenicol, erythromycin and gentamicin (Adzitey et al., 2012b). *Campylobacter species* (*C. jejuni* and *C. coli*) isolated from chickens and turkey exhibited resistances >60% to ampicillin, tetracycline, trimethoprim-sulfamethoxazole and pefloxacin (Nobile et al., 2013). Resistant to ampicillin, ciprofloxacin, erythromycin and nalidixic acid was observed in *C. jejuni* isolated from chickens and guinea fowls (Kilonzo-Nthenge et al., 2008). *Campylobacter lari* was only resistant to ampicillin, kanamycin and nalidixic acid (Kilonzo-Nthenge et al., 2008).

All *Salmonella* serovars isolated from ducks were resistant to erythromycin but susceptible to cephalothin, gentamicin and ceftriaxone (Adzitey et al., 2012b). Ta et al. (2014) reported that chicken meat *Salmonella* isolates showed resistance to at least one antibiotic, with high resistances to tetracycline (59.1%) and ampicillin (41.6%); and resistance to three antibiotics was the most frequently found multidrug resistance profile (17.7%). *Salmonella* isolates from chickens and guinea fowls were resistant to ampicillin, streptomycin and tetracycline (Kilonzo-Nthenge et al., 2008). *Salmonella species* from poultry environmental samples were all resistant to clindamycin, oxacillin, penicillin and vancomycin but susceptible to ampicillin, enrofloxacin and colistin (Singh et al., 2013). Raw chicken carcasses *Salmonella* isolates were resistance to penicillin (100%), oxacillin (97%), clindamycin (97%), vancomycin (92.6%), erythromycin (89.7%), ampicillin (85.2%) tetracycline (67.6%), streptomycin (61.7%), neomycin (55.8%) and cephalothin (52.9%) (Yildirim et al., 2011).

Alvarez-Fernandez et al. (2013) isolated *Escherichia coli* from conventionally and organically reared poultry and reported that, the disc diffusion method showed that 91.7% of the isolates were multi-resistant (resistant to two or more antimicrobials). They also found that resistance to nalidixic acid was the commonest (85.0%), followed by resistance to ampicillin (75.0%), ciprofloxacin (73.3%) and tetracycline (61.7%). All 55 ducks *E. coli* isolates were resistant to vancomycin (Adzitey et al., 2013c). Higher resistance (≥ 60%) to tetracycline (92.7%), ampicillin (72.7%), streptomycin (67.3%) and sulfamethoxazole-trimethophrim (67.3%) also occurred (Adzitey et al., 2013c). *E. coli* isolates were resistant to sulphonamides (68% versus 47.6%), tetracycline (62.5% versus 55%), minocycline (27% versus 26.3%) and nalidixic acid (66% versus 23%) for turkeys and hens, respectively (Cormican et al., 2001). *E. coli* isolates from chickens and guinea fowl were resistant to ampicillin and nalidixic acid (Kilonzo-Nthenge et al., 2008).

The percentage antibiotic susceptibility pattern of Gram positive bacteria isolates from poultry faeces showed 100% resistance to streptomycin, chloramphenicol, ceftriazone, gentamycin and erythromycin; 80% resistance to amoxicillin and cotrimoxazole and 40% resistance to ofloxacin, pefloxacin and ciprofloxacin (Adeleke and Omafuvbe, 2011). While Gram negative bacterial isolates showed above 60% resistance to augmentin, nitrofurantoin, ceftriazone, gentamycin, cotrimoxazole, amoxicillin and tetracycline; and below 30% resistance to ciprofloxacin, ofloxacin and pefloxacin (Adeleke and Omafuvbe, 2011).

Classes, mechanisms and resistance of antibiotics used in poultry production

Antibiotics are chemicals or drugs that kill or slow the growth of bacterial foodborne pathogens. Antibiotics that kill bacteria are referred to as bactericidal and those that slow the growth of bacteria are referred to as bacteriostatic. Antibiotics are part of 'antimicrobials' which include anti-fungal, anti-parasitic and anti-viral drugs. Antibiotics are classified based on their chemical structure, mechanism or spectrum of action (Calderon and Sabundayo, 2007). Classification based on the chemical structure includes the aminoglycosides, cephalosporins, macrolides, quinolones (fluoroquinolones), streptogramins, tetracyclines, sulphonamides and many more. Antibiotics that target the bacterial cell wall (penicillins and cephalosporins), the cell membrane (polymixins), or interfere with essential bacterial enzymes (quinolones and sulfonamides) have bactericidal activities (Calderon and Sabundayo, 2007). Those that target protein synthesis (aminoglycosides, macrolides and tetracyclines) are usually bacteriostatic (Calderon and Sabundayo, 2007). Some antibiotics are also specific and targets either Gram-positive or Gram-negative bacteria (narrow spectrum antibiotics), others target both (broad spectrum antibiotics). Table 1 shows some classes of antibiotics used in poultry production, bacteria types they are commonly used against and mechanisms of action involved. Table 1 indicates that various antibiotics are used to kill or reduce the number of Gram-positive or negative bacterial infections in farm animals.

Table 1. Common use and mechanism(s) of action of antibiotic groups

Antibiotic Group	Examples	Common use (against)	Mechanism(s)
Aminoglycosides	Gentamicin, Kanamycin, Neomycin	Gram negative bacteria	Binding to the bacterial 30S or 50S ribosomal, inhibiting the translocation of the peptidyl-tRNA from the A-site to the P-site and also causing misreading of mRNA, leaving the bacterium unable to synthesize proteins vital to its growth
Cephalosporins			
1st Generation	Cefazolin, Cefalexin, Cefalotin	Gram positive bacteria	Same mode of action as other beta-lactam antibiotics: disrupt the synthesis of the peptidoglycan layer of bacterial cell walls
2nd Generation	Cefuroxime, Cefoxitin, Cefoxitin	Less Gram positive, improved Gram negative	
3rd Generation	Cefoperazone, Cefotaxime, Ceftriaxone	Mainly Gram negative bacteria except Pseudomonas	
4th Generation	Cefepime	Covers Pseudomonas	
5th Generation	Ceftaroline, fosamil, Ceftobiprole	Used to treat MRSA	
Glycopeptides	Vancomycin, Teicoplanin	Gram positive bacteria	Inhibiting peptidoglycan synthesis
Macrolides	Erythromycin, Azithromycin, Clarithromycin	Mostly Gram positive	Inhibition of bacterial protein biosynthesis by binding reversibly to the subunit 50S of the bacterial ribosome, thereby inhibiting translocation of peptidyl tRNA.
Penicillins	Amoxicillin, Ampicillin, Methicillin, Penicillin	--	Same mode of action as other beta-lactam antibiotics: disrupt the synthesis of the peptidoglycan layer of bacterial cell walls
Quinolones	Ciprofloxacin, Nalidixic acid, Norfloxacin, Ofloxacin	Gram positive and negatives	Inhibit the bacterial DNA gyrase or the topoisomerase IV enzyme, thereby inhibiting DNA replication and transcription
Sulfonamides	Sulfamethizole, Trimethoprim/Sulfamethoxazole	--	Inhibit folate synthesis
Tetracyclines	Tetracycline, Oxytetracycline	Gram positive and negatives	Inhibiting the binding of aminoacyl-tRNA to the mRNA-ribosome complex. They do so mainly by binding to the 30S ribosomal subunit in the mRNA translation complex.
Chloramphenicol	Chloramphenicol	Gram positive and negatives	Inhibits bacterial protein synthesis by binding to the 50S subunit of the ribosome

Anonymous (2012a)

Penniclllins

Penicillins kill bacteria by inhibiting formation of the bacterial cell wall causing the wall to breakdown to release the contents of the cell. Penicillins are effective in the treatment of sinusitis and chronic respiratory disease in poultry. Examples of penicillins are amoxicillin and ampicillin (Calderon and Sabundayo, 2007; Anonymous, 2012a and Jacob, 2015).

Cephalosporins

These are also beta lactams antibiotics and structurally closely related to penicillins. Cephalosporins are further divided into first, second, third, fourth and fifth generations with each generation having a wider spectrum of activity than the one before. Cephalosporins interfere with bacteria cell walls by disrupting the synthesis of the peptidoglycan layer of bacterial cell wall. Examples include cefazolin (1st generation), cefoxitin (2nd generation), ceftriaxone (3rd generation), cefepime (4th generation) and ceftaroline (5th generation) (Calderon and Sabundayo, 2007; Anonymous, 2012a and Jacob, 2015).

Aminoglycosides

These antibiotics are made from various species of *Streptomyces*. Aminoglycosides works by obstructing the synthesis of bacteria protein essential for the growth of the bacteria. Their sites of action are the digestive tract and so are effective for combating enteric infections. Spectinomycin, streptomycin, gentamicin, kanamycin and neomycin are examples of aminoglycosides (Calderon and Sabundayo, 2007; Anonymous, 2012a and Jacob, 2015).

Glycopeptides

These antibiotics work by interfering with the production of proteins and the formation of bacteria cell. They disrupts peptidoglycan cross linkage. Glycopeptides are effective against *S. aureus* and *S. epidermidis*. Vancomycin and teicoplanin are examples of glycopeptides (Calderon and Sabundayo, 2007; Anonymous, 2012a and Jacob, 2015).

Macrolides

They can be prepared from *Streptomyces* bacteria. Macrolides of *Streptomycin species* origin are bacteriostatic and works by interfering in the production of bacteria protein binding of 50S. Macrolides are effective against *Mycoplasma, pneumonia, Haemophilus influenza* and *Orhnithobacterium* via reversible *rhinotracheale* and can be used to treat necrotic enteritis. Examples are azithromycin, clarithromycin and erythromycin (Calderon and Sabundayo, 2007; Anonymous, 2012a and Jacob, 2015).

Sulfonamides

They are mainly produced by chemical synthesis and bacteriostatic against a broad spectrum of pathogens. Sulfonamides inhibit DNA and RNA synthesis. DNA and RNA are essential for cell replication and growth. Sulfonamides are effective against *Staphylococcus species*, *Streptococcus species*, *Salmonella species* and *E coli*. Trimethoprim and sulfamethizole are examples of sulfonamides (Calderon and Sabundayo, 2007; Anonymous, 2012a and Jacob, 2015).

Fluoroquinolones

These are synthesis antibiotics and have broad spectrum bactericidal effect. Fluoroquinolones are also further divided into first, second, third and fourth generations with each generation having a wider spectrum of activity than the one before. They prevent bacteria from multiplying by stopping them from making DNA through inhibition of DNA gyrase. Examples of fluoroquinolones are nalidixic acid (1^{st} generation), ciprofloxacin (2^{nd} generation), gatifloxacin (3^{rd} generation) and moxifloxacin (4^{th} generation). Fluorquinolones are effective against salmonellosis, colibacillosis and fowl cholera (Calderon and Sabundayo, 2007; Anonymous, 2012a and Jacob, 2015).

Tetracyclines

Most of them are derived from *Streptomyces species* and have broad spectrum bacteriostatic effects. They prevent bacteria from multiplying by blocking tRNA, while the host animal's immune system deals with the original infection. Tetracyclines are effective against *Mycoplasma, Clostridium* and some protozoa (Calderon and Sabundayo, 2007; Anonymous, 2012a and Jacob, 2015).

Emergence of resistant bacterial foodborne pathogens to antibiotics reflects evolutionary processes that take place as animals are expose to antibiotics (Witte, 2004 and Levy, 1994). The antibacterial treatment may select for bacterial strains with physiologically or genetically enhanced capacity to survive high doses of antibiotics which can result in preferential growth of resistant bacteria, while the growth of susceptible bacteria is inhibited (Levy, 1994). Resistant of bacterial foodborne pathogens to antibiotics can also occur by inheritance that is horizontal gene transfer, which is more likely to happen in locations of frequent antibiotic use (Dyer, 2003 and Witte, 2004). Intrinsic antibacterial resistance may be part of the genetic make-up of the bacterial strain e.g. by not having an antibiotic target in it bacterial genome (Alekshun and Levy, 2007). Acquired resistance results from a mutation in the bacterial chromosome or the acquisition of extra-chromosomal DNA (Alekshun and Levy, 2007). Antibacterial resistance genes can be exchanged between different bacterial strains or species via plasmids that carry these resistance genes and plasmids that carry several different resistance genes can confer resistance to multiple antibacterials (Alekshun and Levy, 2007; Baker-Austin *et al*., 2006).

Farm practices such as feeding, breeding and treatment of sick animals are the main contributory factors to the use of antibiotics in animal husbandry (Aarestrup et al., 2008; Adzitey et al., 2012c). Antibiotics are sometimes used in animal feeds as growth promoters and to increase performance. Currently, chlortetracycline, procaine, penicillin, bacitracin, neomycin, oxytetracycline, sulfate, streptomycin and erythromycin are among the antibiotics used in livestock and poultry feeds (Anonymous, 2012b). Anonymous (2012b) also stated that, the reasons for using these antibiotics are to promote efficient conversion of feed to animal products, to increase growth rate and to lower morbidity/mortality rate. Furthermore, antibiotics are used to treat animals when they are ill or given to animals to prevent them from falling sick.

CONCLUSION

Antibiotics are essential in poultry production. However, excessive and indiscrimate use of antibiotics will lead to the development of bacterial isolates that are multidrug resistance. Therefore, antibiotics should only be used when

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necessary. It is very important to strictly follow the manufacturers' instructions in the administration of antibiotics during treatment of farm animals.

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