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Research Article

Antibacterial Agents Common in Poultry Drug Formulations from Multi-Sources Available in Nigeria

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Abstract

This study was designed to develop a list of antibacterial drugs that are commonly included as active ingredients in the available fixed-dose multisource formulations (FDMF) for poultry use in Nigeria. This will be a template in choosing drugs for culture and sensitivity tests in order to optimize therapeutic outcomes in poultry practice. Sampling was done in the study areas simultaneous between January 2016 and December 2018. Also, samples were obtained exclusively from poultry farms (n = 37), veterinary (n = 23), and pharmaceutical (n = 2) stores. Results showed that 31 different antibacterial agents from 7 antibacterial classes were included in the 468 FDMF for poultry use in Nigeria. The most common classes of antibacterial drugs were the tetracyclines, sulphonamides and aminoglycosides. Again, oxytetracycline (a tetracycline), doxycycline (a tetracycline), and neomycin (an aminoglycoside) were the most common antibacterial agents, and included in 19%, 12%, and 11%, respectively of the 468 FDMF sampled. Most of the commonly included antibiotics in the 468 FDMF are medically important for human as well, hence a potential adverse effect on public health due to emergence of resistant bacterial organisms. There is therefore a need to limit the use of antibiotics with clinical relevance for human in poultry practice. Also, the choice of antibacterial sensitivity test should be based on the common antibiotics in the available fixed-dose formulations.

Keywords: *Antibacterial Drugs; Fixed-Dose Formulations; Culture And Sensitivity Tests; Poultry Practice; Nigeria*

Introduction

Antibacterial agents are natural, synthetic, or semi-synthetic chemical substances that kill or inhibit the growth of bacterial organisms [1]. They are often used in the prevention and treatment of bacterial infections in animals, including poultry notably fowl coryza (*Avibacterium paragallinarum*), fowl typhoid (*Salmonella spp*), and fowl cholera (*Pasteurella multocida*) among others. These formulations are usually administered in drinking water, but rarely by intramuscular route of administration. One of the major problems militating against profitable poultry production are the infectious diseases, particularly bacterial infections which are most common in the tropics, including Nigeria. As a result, the rate and extent of antibacterial use in poultry in the tropical regions is high with consequent increased cost of production. In Nigeria, Adejoro [2] estimated that poultry farmers spend over 35% of the total cost of production in the prevention and treatment of bacterial diseases.

According to the World Health Organization [3], more than 80% of antibacterial agents from multi-sources are used in veterinary medicine to prevent or treat bacterial diseases in animals as well as to enhance growth in food animals. Most of these drugs are used

in poultry (chickens) and pig production across the world. In addition, a report from United State Food and Drug Administration (FDA) showed that several of these antibacterial drugs used in the treatment of bacterial diseases in animals are also prescribed for human patients [4]. Consequently, the critical role of antibacterial drugs in both animal and human health cannot be overemphasized.

One of the requirements for prudent use of antibacterial drugs is that the sensitivity of the incriminating bacterial organism in a diagnosed disease to the antibacterial drug of choice must be ascertained to circumvent drug resistance as well as to optimize the desired clinical outcomes [5]. The selection of antibacterial agents for this sensitivity test must be based on their availability and inclusion in the Fixed-Dose Multisource Formulations (FDMF) available in the region under consideration. Presently, there is no data in Nigeria and most developing countries on the antibacterial agents commonly included in the array of FDMFs, particularly for poultry use. Therefore, antibacterial sensitivity tests and studies are most often based on the available commercial discs impregnated with antibacterial agents, most of which are not available as active pharmaceutical ingredients (API) in the commonly marketed and used FDMF for poultry use. The clinical implication is that, most often, the best potentially effective drugs based on culture and sensitivity results are not available for use because of their non-inclusion in the available FDMFs. This often renders most of the culture and sensitivity studies in avian practice a mere academic exercise. Subsequently, this study was designed to develop a list of antibacterial drugs that are commonly included as APIs in the available FDMFs in some parts of Nigeria in order to guide the choice of drugs for culture and sensitivity tests in the veterinary clinics or clinical researches for optimal treatment outcomes.

Materials and Methods

Study locations

The study was conducted in five states of Kaduna, Benue, Oyo, Enugu, and Delta representing north-west, north-central, south-west, south-east, and south-south geopolitical regions of Nigeria, respectively. The choice of these locations was informed by high extent of poultry farming and consequently poultry practice in those states as compared to other states within the geopolitical zone. In addition, Ibadan the capital city of Oyo state is considered as the hub of poultry practice in south-west in particular and Nigeria as a whole.

Data sampling

A survey of FDMF for poultry use was carried out in the study areas. Information from these FDMF extracted included their APIs, manufacturing/expiry dates, indications, dosage regimens, National Agency for Food and Drug Administration (NAFDAC) registration number, and countries where these products were produced. We also ensured that no product from the same company, same API(s) of same labelled amount and formulation was recorded twice even when it was found in one or more veterinary or pharmaceutical shops or poultry farms from one or more sampled locations. Sampling was done in the study areas simultaneous between January 2016 and December 2018. Also, the samples were obtained exclusively from poultry farms (n = 37), veterinary (n = 23), and pharmaceutical (n = 2) stores.

Data analysis

Simple statistical analyses were conducted using Excel (2016) to evaluate the frequencies of different classes and individual antibacterial agent(s) in the different products sampled. The ranking (%) of countries based on the drug products produced, the percentage of drug products that has the dates of manufacture and expiration, as well as NAFDAC registration numbers indicated on their labels were evaluated.

Results

Figure 1 shows that out of 468 FDMF containing antibacterial agents sampled in the study locations, 34%, 20%, 18%, and 11% contained tetracyclines (TETS), sulphonamides (SUMS), aminoglycosides (AMGS), and macrolides (MCLS) classes of antibacterial drugs, respectively as APIs. Whereas 3% of the products contained chloramphenicol (CAMS), while β-lactams (BLMS) and fluoroquinolones (FLQS) each were found in 7% of the products. Apart from the sulphonamide class, none of the FDMF contained more than one antibacterial agent from the same class. Out of 158 different available FDMF containing the tetracyclines (Figure 2), 58% contained oxytetracycline (OTC) while 35% contained doxycycline (DOC) as APIs.

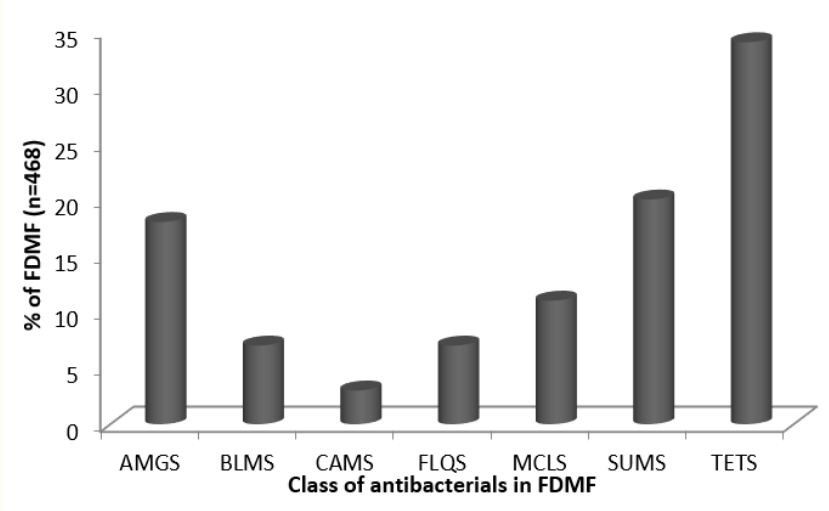

Figure 1: *Common classes of antibacterial agents in the available FDMF (n = 468) for poultry use.*

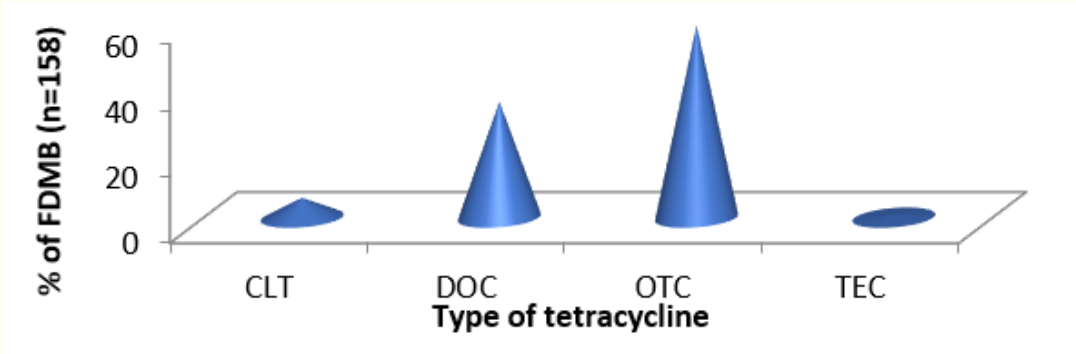

Figure 2: *Tetracyclines contained in different FDMF (n = 158) for poultry available in some parts of Nigeria.*

Figure 3 illustrates that of the 85 aminoglycosides included in sampled different brands of drug formulations for poultry, 62%, 26%, and 11% contained neomycin (NEO), streptomycin (STP), and gentamicin (GEN), respectively. Result also showed that, out of 32 FDMF with β-lactams, 41% and 37% contained ampicillin (AMP) and amoxicillin (AMX), respectively (Figure 4). In addition, cloxacillin (CLX) and penicillin (PEN) were found in only 16% and 6%, respectively of the brands containing β-lactams. Again, figure 5 shows different fluoroquinolones and their presence as APIs in 34 FDMF available for poultry use in some parts of Nigeria. Result demonstrated that 47%, 26%, and 21% of the available FDMF containing fluoroquinolones had enrofloxacin (ENR), ciprofloxacin (CIP), and flumequine (FLU), respectively. Results presented in figure 6 shows that out of the 51 FDMF with macrolides, erythromycin (ERYT) and tylosine (TYLO) were present in 49% of these products.

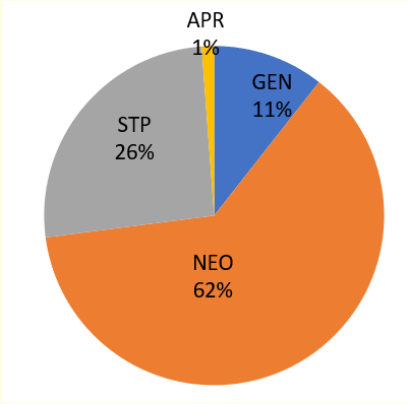

Figure 3: *Individual aminoglycosides in the available FDMF (n = 85) for poultry use in some parts of Nigeria.*

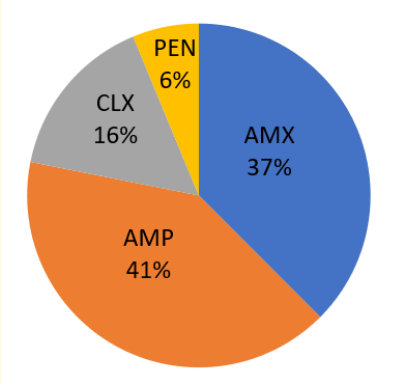

Figure 4: *β-lactams contained in available FDMF (n = 32) for poultry use in some parts of Nigeria.*

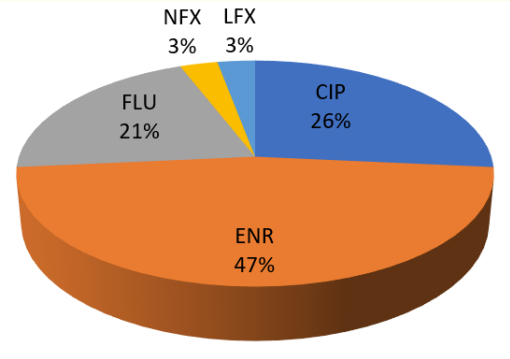

Figure 5: *Fluoroquinolones in some FDMF (n = 34) for poultry use in parts of Nigeria.*

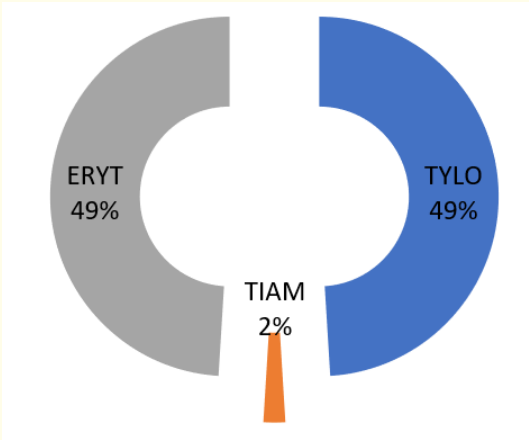

Figure 6: *Macrolides found in the 51 sampled FDMF for poultry use in some parts of Nigeria.*

Furthermore, figure 7 shows that out of 96 FDMF for poultry use that contained sulphonamides, 27% and 20% contained sulphaquinoxaline (SQX) and sulphadimidine (SDD), respectively; while trimethoprim (TMTP) and sulphadiazine (SDZ) were found in 14% of the FDMF. Results presented in figure 8 indicates that 67% of the FDMF for poultry use that contained chloramphenicol had chloramphenicol (CAM), while 33% of them contained florfenicol FCO). Result presented in figure 9 shows that 31 different antibacterial agents were found in the 468 FDMF available for poultry use in the study locations. Oxytetracycline was the most commonly included antibacterial agents in these formulations whereby 18% of them contained it as one of the APIs. Also, doxycycline and neomycin were found in 12% and 11%, respectively of the available FDMF. A total of 18 antibacterial agents (Others) found in the FDMF sampled were included as API in < 2% of the sampled FDMF (17%).

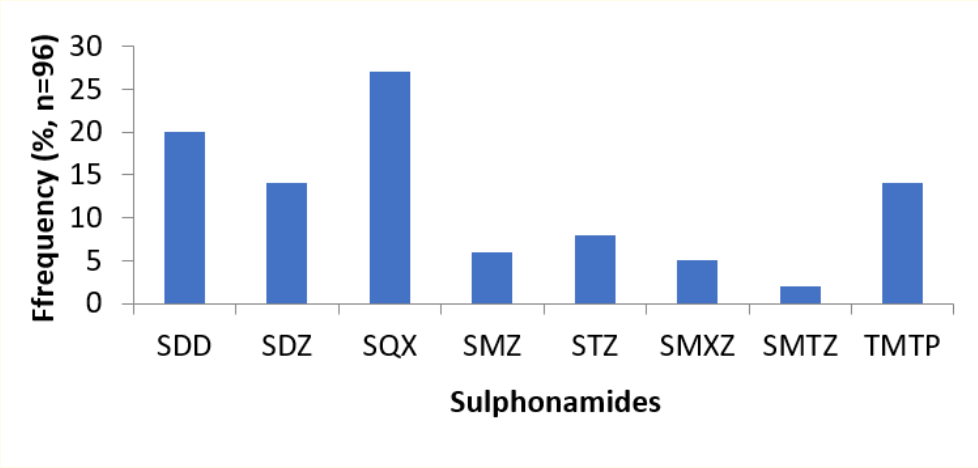

Figure 7: *Sulphonamides as active ingredients in 96 FDMF available in parts of Nigeria.*

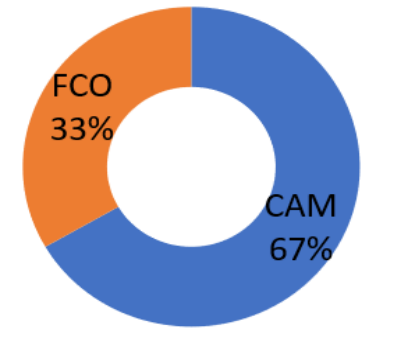

Figure 8:*Two chloramphenicol in the 12 FDMF sampled in some parts of Nigeria.*

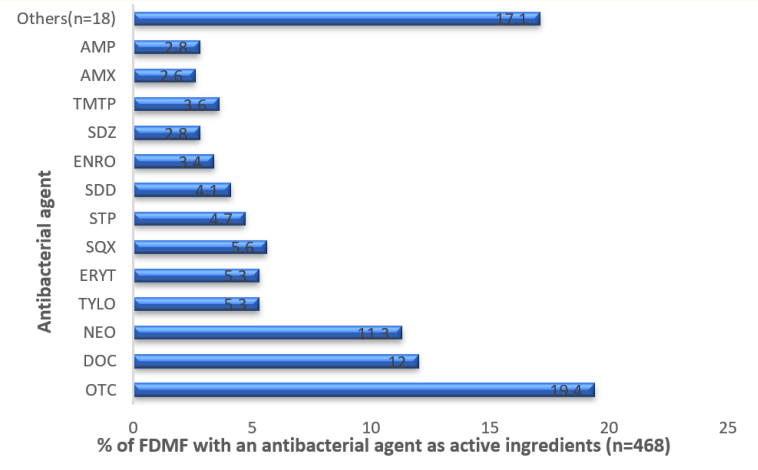

Figure 9:*Frequency of different antibacterial agents in sampled FDMF available in parts of Nigeria.*

Figure 10 shows that 29%, 19%, and 9% of the 468 FDMF were produced in Nigeria (NIG), Holland (HOL), and China (CHI). However, the manufacturers of 5% of the FDMF did not indicate their country of production (XXX). Out of the 468 FDMF sampled, 22% were registered with NAFDAC as indicated on the product package, whereas 78% were not registered (Table 1).

Indices	Yes (%)	No (%)
NAFDAC Reg.	101 (22)	367 (78)
Batch No.	120 (26)	348 (74)
Manufacturing date	352 (75)	116 (25)
Expiry Date	340 (73)	128 (27)
Contents/amount	468 (100)	0 (0)
Indications stated	468 (100)	0 (0)
Dosage regimen	420 (90)	48 (10)

Table 1*: Compliance with regulations and labelling by manufacturers of the FDMF for poultry use (n = 468).*

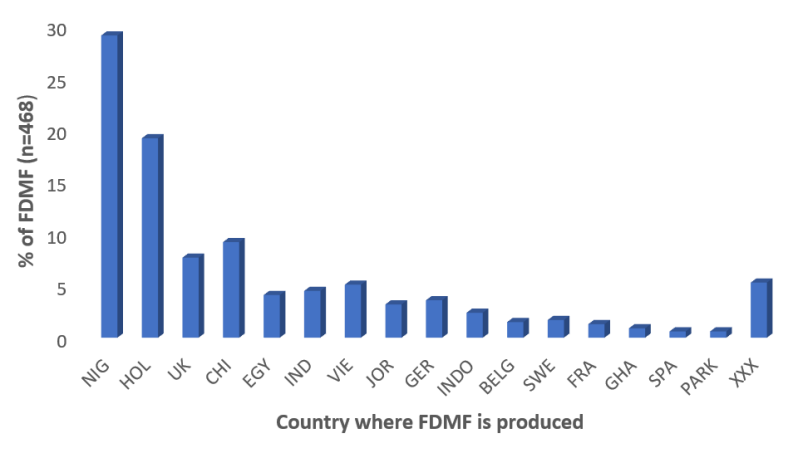

Figure 10 :*Sources of different FDMF sampled from different locations in Nigeria.*

Discussion

The rate and extent of antibacterial drugs use in food animals, including poultry to treat and/or prevent bacterial diseases as well as to promote growth is more than their use in the entire human population [4]. Because of the high prevalence and risks associated with bacterial diseases as compared with other challenges in poultry production in the tropics, a larger percentage of the production cost is incurred by poultry farmers on the purchase of antibacterial drugs to circumvent these [2]. This study revealed that 31 different antibacterial agents from 7 antibacterial classes were included in the 468 multisource fixed-dose formulations for poultry use available in some parts of Nigeria. The most common classes of antibacterial drugs were the tetracyclines, sulphonamides, and aminoglycosides; where oxytetracycline (a tetracycline), doxycycline (a tetracycline), and neomycin (an aminoglycoside) were the most common antibacterial agents and included in 19%, 12%, and 11%, respectively of the 468 multisource fixed-dose formulations sampled.

Fowl typhoid, fowl cholera, fowl coryza, and chronic respiratory disease caused by *Salmonella spp*, *Pasteurella spp*, *Avibacterium paragallinarum*, *Mycoplasma spp*, and *E. coli*, respectively were reported to be the most prevalent bacterial diseases affecting poultry production in Nigeria [6]. The same authors in same study reported that doxycycline and oxytetracycline were the most frequently prescribed drugs for treating these conditions. This corroborates our finding in this study that oxytetracycline and doxycycline are the two most common antibacterial agents in the array of fixed-dose formulations marketed in Nigeria for poultry use. In addition, tylosine and erythromycin (macrolides), streptomycin and gentamicin (aminoglycosides), amoxicillin and ampicillin (β-lactams), enrofloxacin and ciprofloxacin (fluoroquinolones) were among the 11 most common antibacterial agents included in the array of available fixed-dose drug formulations from multisource for poultry use in some parts of Nigeria.

Most of the therapeutic failures following the use of antibacterial agents occur when the pathogenic bacterial organism is unknown and combination of two or more antibacterial drugs administered empirically. To circumvent these inaccuracies, clinically confirmed effective antibacterial agent or combinations is required [7]. This informs the need for culture and sensitivity tests in order to prudently select the antibacterial agent or a combination that will produce the desired therapeutic outcome. Out of the 13 antibacterial agents reported in this study (Figure 9) to be often included in the available fixed-dose formulations for poultry use, only 6 (doxycycline, neomycin, amoxicillin, ampicillin, and erythromycin) of them are commonly used for susceptibility tests for clinical bacterial isolates from poultry [8-11]. Most of the antibacterial agents coated on the available susceptibility tests discs used in the veterinary clinics and poultry researches are not formulated for animal use, particularly for poultry explaining why most of the commonly used poultry antibacterial

drugs are not included. Also, despite the fact that oxytetracycline is the most commonly included antibacterial drug in the array of multi-source formulations as well as commonly used, it is not usually included in the list of antibacterial agents for culture and sensitivity tests.

Drug products labelling is one of the key indices of quality assessment of pharmaceutical products. Drug labeling refers to all the printed information that accompanies a drug, including the label, the wrapping and package insert [12]. The label on a pharmaceutical product must contain the product's name, active ingredient (s), batch number, manufacture/expiry dates, indications, dosage regimen, address of the manufacturer and/or distributor, and the country of origin [13,14]. Results revealed that 27%, 74%, and 78% of the 468 fixed dose formulated commercial products were not labelled properly in respect of their expiry date, batch numbers, and NAFDAC registration. This shows that the quality of these pharmaceutical products is questionable, corroborating the report that antibiotics are among the most counterfeited and substandard drugs in Africa and Asia, with the oral formulations topping the list [15].

Conclusion

This study revealed that most of the antibiotics used in poultry in Nigeria are clinically important human antibiotics, consequently a potential danger to public health resulting from drug resistance. Also, most of the commonly used antibiotics in poultry medicine are not usually included in culture and sensitivity tests in poultry clinics and researches. There is therefore the need to limit the inclusion of antibiotics that are clinically relevant in humans into poultry formulations. Again, the choice of antibiotics for sensitivity studies should be based on the types commonly included in the available formulations for poultry and which are commonly used in poultry farms.

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