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Veterinary Drug Residues in Meat and Meat Products: Occurrence, Detection and Implications

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Abstract

Application of veterinary drugs in livestock production is inevitable as they are essential for treatment of diseases, prevention of diseases, modification of physiological functions, improvement of growth and productivity as well as for ensuring food safety. However, recent reports have revealed that the use of veterinary drugs in large amounts and consistently could result in deposition of antimicrobial residues in muscle and organs of animal. Consumption of these residues in animal products may pose health risk to consumers including development of antibiotic resistance bacteria, allergy, reproductive disorder and hypersensitivity reaction. It is in line with this that this chapter seeks to examine the cause, occurrence, mode of detection, health implication and possible solution to veterinary drugs residues in meat and meat products.

Keywords: antimicrobial residue, meat and meat product, veterinary drugs, consumers' health, antimicrobial resistance

1. Introduction

The use of veterinary drugs in livestock production is inevitable as they are essential for treatment of diseases (therapeutic), prevention of diseases (prophylaxis), modification of physiological functions (such as tranquilizers, anesthetic drugs), improvement of growth and productivity (growth promoters) as well as for ensuring food safety [1]. The veterinary drugs are used throughout the world and they comprise a broad variety of classes of chemical compounds including vaccines, antimicrobials, antiparasitics and β -agonists [2]. These drugs have been used to strengthen profitability and productivity of modern food-animal production by facilitating earlier weaning, higher animal densities, carcass yield and meat quality as well as the use of cheaper feed sources [2]. Among the antimicrobials that are commonly used in livestock production are tetracyclines, amprolium, penicillin, streptomycin, sulphonamides, tylosin, aminoglycosides, β -lactams, macrolides and lincosamides, quinolones, sulfonamides and tetracyclines [3, 4] while that of antiparasitic agents include anthelmintics or coccidiostats, stilbenes, amphenicols, nitrofurans, nitroimidazoles, carbamates, pyrethroids and sedatives.

Antimicrobials are medicine (natural, synthetic or semi-synthetic origin) that inhibits the growth of or destroys microorganisms when applied at low

concentrations without causing host damage [5]. In the course of this study, “antimicrobial” will be considered an equivalent term to “antibiotic”. Many antimicrobials that are used in livestock are identical or closely related to antimicrobials used in humans. Most of the antimicrobials use in livestock can lead to development of antimicrobial-resistant bacteria in muscle food, which can then be transmitted to humans via food and other transmission routes [1].

At present the global average annual consumption of antimicrobials per kilogram of animal produced is estimated at >100 mg/kg [6]. It has also been showed that about 80% of all the antibiotics administered in veterinary field are used as growth promoters and in most cases, this exceeds the total antibiotics use for human medical care [6]. In a study, Aarestrup [7] observed that global consumption of antibiotic in animals is twice that of humans. In fact, in developed countries like USA, Food and Drug Administration [8] reported that about 80% of countries total antimicrobial consumption are used in food animals. On estimate, Van Boeckel et al. [9] found that about 45, 148 and 172 mg/kg of antimicrobial per animal are used annually for cattle, chicken and pig production globally, respectively. It has been predicted that global consumption of antimicrobial by livestock will increase 67% from 63,151 tons in 2010 to 105,596 tons by 2030 [9].

However, recent reports have revealed that the use of antimicrobial drugs in large amounts and consistently could result in deposition of antimicrobial residues in muscle and organs of animal [10]. Consumption of these residues in animal products (especially through meat and meat products) may cause health risk to consumers including development of antibiotic resistance and hypersensitivity reaction. FAO/WHO reported that antimicrobial residues edible animal products has grown beyond permissible level (very high) is in developing countries [11]. In order to curtail this, the European legislation has set maximum residue limits for veterinary drug residues in different animal food products (European Commission Council Regulation (EEC), [12]). Nisha [13] highlighted that the maximum veterinary residue limits for tetracycline, oxytetracycline, streptomycin, gentamicin, sulphonamides, quinolones, among others, to be 100, 100, 200, 200, 100 and 75 µg/kg respectively. It is therefore imperative that animal products (particularly meat and milk) should be analyzed to ensure that residues do not exceed maximum residue limits. Since unintentional consumption of antimicrobial residues in food products leads to drug resistance of bacteria that are pathogenic to humans with consequence of serious threat to human health [14]. It is in line with this that this chapter will focus on recent findings on causes, occurrences, mode of detections, health implication and possible solution to veterinary drugs residues in meat and meat products.

2. Drivers of antimicrobial residues in meat and meat products

2.1 Outbreak of livestock diseases

Livestock production is one of the fastest growing agricultural sectors in most countries of the world. However, the health and growth of this livestock are plagued by many diseases caused by different infectious microorganisms globally. The past decade has seen the rise of many new diseases, with more of new potential pathogens anticipated to occur by 2020 [15, 16]. The outbreak of infectious microorganisms has necessitated widespread use of antimicrobial drugs to protect and maintain the health of the animal during production and also ensure safe food after harvest. Since animals that are sick and untreated grow more slowly and may eventually results in mortality, imposing a considerable economic burden on producers

and government by dramatically reducing income and means of livelihood to farm owner and workers [17]. In treatment and prevention of these diseases, FAD [18] observed in a study that 60% of domestic sales and distribution of medically important antimicrobials in year 2016 were used in food-producing animals in United States. Of this estimate, the same author reported that Tetracyclines accounted for 70% of these sales, penicillins for 10%, macrolides for 7%, sulfas for 4%, aminoglycosides for 4%, lincosamides for 2%, and cephalosporins and fluoroquinolones each for less than 1%. Often time, the amount of antimicrobial use in livestock depends on the number of animals, the production system, prevailing risk factors for disease and ability to acquire antimicrobial agents income [17]. However, misuse or excessive use of antimicrobials among livestock and in adherent to withdrawer time has resulted to spread of antimicrobial residues (either the parent compound or its metabolite) in muscles especially meat and meat products [19, 20].

The occurrence of antimicrobial residues in muscle food pose a risk to human health by being acutely or cumulatively allergenic, organotoxic, mutagenic, teratogenic or carcinogenic [11]. In fact, report has shown that antimicrobial resistant bacteria can represent a reservoir of resistance genes transferable to pathogenic or commensal bacteria in digestive tract [21], and therefore compromise the effective treatment of bacterial infections. This could be a serious threat to disease treatment in humans and animals. Therefore, it is imperative that precise antimicrobial drugs be used in livestock production for overall decrease in animals suffering due to infectious diseases.

2.2 Excessive demand for meat and meat products

Meat represents a substantial portion of the diet of most people worldwide. Its consumption has significant health benefits as good source of proteins, essential amino and fatty acids, vitamins and minerals and other bioactive compounds [22]. The worldwide average meat consumption is estimated at 42.9 kg per capita, with industrial countries consuming about 76.1 kg, twice the quantity in developing countries (33.6 kg) [23, 24]. However, it has been indicated that the consumption of meat and meat products will double by 2050. Meat consumption will continue to expand due to increase in population growth across the world, with the developing world having most demand growth over the coming decades [25]. In an attempt to produce sufficient meat to meet this demand, antimicrobials are being increasingly used for the treatment of livestock diseases and increase productivity (growth promoters). Currently, more than 300 antimicrobials, anti-coccidials, feed additives and hormone-type agents are used in livestock production globally [26–28].

According to OECD/FAO [25] statistic, about 323 metric tons of meat was produced globally in 2017 and this has been projected to be 15% higher in 2027. Most of this increase in the next decade will emanate due to higher demand in beef and sheep meat than poultry and pig meat [25]. It has also been reported that much of the increase in production will originate from United States, India, Argentina, Mexico, China, Turkey and the Russian Federation. Report has showed that the increase in antimicrobial consumption is due to the growing number of animals raised for food production coupled with increase in consumer demand for livestock products including meat and meat products [9]. On average, worldwide consumption of antimicrobials in food animal production was estimated at 63,151 (± 1560) tons in 2010 and by 2030, it has been projected to increase by 67%, to 105,596 (± 3605) tons or even double in countries such Brazil, India, Russia, South Africa and China [9]. In Asia for instance, antimicrobial consumption in chicken and pig production has been projected to grow by 129% and 124%, respectively, by 2030 [9]. Antimicrobial resistant strains have been isolated in food animals in both

the developed and developing countries especially where the use of antimicrobials for growth promotion remains largely unregulated [19, 29]. Skockova et al. [29] in their study found that some strains of *Escherichia coli* isolated from retail meats (pork, poultry, beef, venison) were resistant to one or more groups of antimicrobial agents (tetracycline, b-lactams and quinolones) [29]. In addition, Moniri and Dastehgoli [30] isolated a *fluoroquinolone-resistant Escherichia coli* from broilers due to their exposure to fluoroquinolones drugs. Because of use of antimicrobial drugs in livestock production, bacteria originating from food animals frequently carry a resistance to a range of antimicrobial agents, including those commonly used in humans [29, 31].

2.3 Other important drivers

Beyond above-mentioned drivers, other factors that could be responsible for antimicrobial resistance in meat and meat products include improper dosage of antimicrobials, non-enforcement of laws regulating antimicrobial usage in livestock, weak financial status of livestock farmers, low education and expertise of farmers, and husbandry system (intensive and extensive) [4]. For instance, Alhaji et al. [4] in a study found that majority of the poultry famers did not practices or comply with antimicrobial withdrawal periods before slaughter or marketing of their product for consumption. Noncompliance with antimicrobials withdrawal periods could create low therapeutic doses and high concentration of antimicrobial residues in meat products. By law, animals given an antibiotic should not be processed until the withdrawal period ends. Good management, which includes good hygiene and sufficient feed, can reduce the chances of animals getting disease, hence use of antibiotics. Others include illegal sale of veterinary prescription drugs, marketing or slaughtering of treated/medicated animals intended for rendering purposes, inadequate animal identification and traceability system especially in developing countries [2].

3. Implications: impact on consumers' health and economy

Residual amounts of antimicrobials, antibiotics or their toxic metabolites found in meat, organs or other products such as milk and egg of food producing animals after slaughtering is called veterinary drug residues [32]. Consumption of such food products poses a major health risk due to the failure of treatment following the development of resistant microorganisms [33]. Various impacts of antimicrobial residues on human health are reported below.

3.1 Impact on consumers' health

3.1.1 Drug resistance

The possibility of propagating resistant bacteria through the food chain in treated animals was noticed as early as 1969 by Swan, who reported the development of vancomycin resistance to *Enterococci* in avoparcin fed animals. Animal feeds containing antibiotics, have been reported to result in antimicrobial resistance, leading to failure of medical treatment both in animals and humans. Situations whereby drugs are completely ineffective have also been reported to be a possibility [34]. Giving the established fact of an animal to human microbial resistance transfer [35], resistant micro-organism can gain entrance, directly through contact, into

humans or indirectly via animal products and by-products (e.g. milk, egg, etc.). The findings of [36] in a study conducted in Taiwan from slaughtered pigs revealed the rate of antimicrobial resistance to salmonella for these drugs; tetracycline (88.2%), gentamycin (82.7%), chloramphenicol (54.3%), amoxicillin (34.6%), nalidixic acid (30.7%), ampicillin (26.8%), kanamycin (18.1%), cephalothin (7.1%), nitrofurantoin (6.3%), ciprofloxacin (0.8%) [36]. Failure of antimicrobial therapy due to resistant strain is a future concern [13].

3.1.2 Allergy or hypersensitivity reactions

Allergy or immune-mediated response to a chemical agent (e.g. drug) can develop in a sensitized patient. Such allergic reactions are usually mediated by IgE and could be elicited following administration of drugs or macromolecules such as protein, lipids and carbohydrates. Dayan [37] affirmed that human population estimate of about 4–11% are believed to be allergic to penicillin. Such class of humans consuming meat products having penicillin residues is at risk of developing allergy which can manifest as a skin rash or even severe anaphylaxis [35]. Thong and Tan [38] reported that IgE-mediated allergic anaphylaxis is linked to penicillin and other anesthetic drugs following their administration during perioperative periods. Mild rash to severe toxidermia are some of the skin reactions following human exposure to sulfonamide [39]. However, such adverse reaction was not a direct effect of consuming animal products containing relative trace amounts of sulfonamides. Studies have also shown that damages done to hepatic liver cells can be traced to allergic response to macrolide antibiotics (e.g. erythromycin, clarithromycin) [40].

3.1.3 Carcinogenic effect

The term carcinogenic refers to any substance or an agent capable of altering the genetic makeup of an organism so that they multiply and become rancorous while carcinogen refers to any substance that promotes carcinogenesis, the formation of cancer or having carcinogenic activity. Carcinogenic residues functions by covalently binding intracellular components including DNA, RNA, proteins, glycogen, phospholipids and glutathione [49]. The ban of Diethylstilbestrol (DES), an hormone-like compound used for food producing animals, was as a result its strong carcinogenic effect [27]. According to the International Agency for Research on cancer (IARC), evidence abounds to suggest that metronidazole is carcinogenic in animal, but insufficient to do so in humans [41].

3.1.4 Disruptions of normal intestinal flora

Intestinal microflora plays an important role in human physiology. They establish control and prevent the colonization of pathogenic bacteria in the gastrointestinal tract [42]. However, studies have shown that antimicrobials administered for therapeutic purposes can potentially alter or change the ecological composition of the intestinal flora [43, 44]. Degree of change however, depends on the dosage of the antimicrobial drug, route of administration, its bioavailability, metabolism, exposure length to the drug and distribution in the body including excretion route [45]. Disruption of intestinal flora has been reported due to the use of broad-spectrum antibiotics. Commonly used drugs like streptomycin, tylosin, metronidazole, nitroimidazole and vancomycin are commonly implicated in human in the diagnosis of gastrointestinal disorders [46].

3.1.5 Mutagenic effect

Mutagens are chemicals or substances with potentials to cause mutations in a DNA molecule thereby altering the genetic makeup of a cell or organism. Studies have shown alkalinizing agents and analogues of DNA bases are mutagenic. There is a growing fear of a possible drug-related gene mutagen or chromosome breakage among human population [47, 48].

3.1.6 Teratogenic effect

Congenital malformation of the foetus during pregnancy as a result of toxic metabolites of drugs or chemical agents has been reported [47]. Such drugs or teratogens alter the structural and functional integrity of the developing embryo/foetus during the critical phase of gestation. Studies have shown that benzimidazole (an anthelmintic) is not only mutagenic but also has teratogenic activities and is highly toxic to embryo when ingested at early stages of conception or pregnancy [49, 50].

3.2 Impact on global economy

Antimicrobials' usage in livestock either at sub-therapeutic or therapeutic dosage and its attendant residues in food animals have become a global issue and concern. The growing awareness about the potential risk of diseases such as cancer and also the distortion of body's functional and system integrity (i.e. endocrine, nervous, reproductive and immune system) [51], resulting from the consumption of such 'compromised' food of animal origin, have reduced consumers' confidence and the resultant adverse impact on global economy. Additionally, the maximum residual limits (MRLs) set by Codex Alimentarius Commission (Codex) for veterinary drug residues as an international food safety standards are however not generally accepted by the committee of nations [52]. The limitation of Codex and World Trade Organization (WTO) to enforce adoption of MRLs [53], has resulted in differences in food safety standards across countries and nations. Such differences usually end as trade disputes [54] leading to a gradual decline in meat and meat products exported.

4. Detection: mode of examination and equipment or methodologies

Studies are replete with developments of antimicrobial resistance from food producing animals after consumption. There is also a general upsurge in form of sensitization on the need to minimize exposure to antibiotic residues in food [55, 56]. Antimicrobial residues in meat and meat products are the results of non-compliance of withdrawal periods, antibiotics overdosing and the continuous use of antibiotics banned for treatment of economic animals [57, 58]. Giving the foregoing above, specific legislation has been set to protect consumers from exposures to potentially harmful residues of veterinary medicines, pesticides and environmental contaminants in food of animal origin. Maximum residual limits (MRLs) have been set for veterinary medicines, pesticides and environmental contaminants (European Regulation (EC) No 470/2009). The Regulation not only seeks to identify but also demand quantitative assessment of antibiotic residues.

Control of antibiotic residues in food of animal origin follows two basic steps: Firstly, the animal product is screened qualitatively or quantitatively. In qualitative

assessment, the presence of an antimicrobial residue is detected here and it's usually reported as either positive or negative. Identification and quantification of a particular residue is done using the quantitative screening method and it is also reported as a concentration of the residue. If results are positive, a confirmatory procedure is usually followed for specific antibiotics with the aid of a more sensitive physic-chemical method.

4.1 Microbial screening method

Though its use dates back as early as 1964 and was adopted initially to monitor the dairy industry with a view to preventing problems in the fermentative dairy industry, it has now been extended as a regulatory residue screening method in slaughter animals even till date. The microbial inhibition assay can cover an entire antibiotic spectrum under one test.

The microbial inhibition assay adopts either the tube test or the plate test. The tube test makes use of a tube, vial or an ampule containing a growth medium inoculated with (spores of) a sensitive test bacterium, supplemented with a pH or redox indicator. At the appropriate conditions of temperature and pH, there is a color from the acid produced by the growing bacteria. Absence or delay of the color change is indicative of the presence of an antimicrobial residue and is usually a commonly used routine in the milk industry [59, 60]. It has however been used for analysis of other matrices [61, 62]. In the plate test, the test sample is spread on the layer of the plate containing inoculated nutrient agar. Presence of an antimicrobial residue is detected by the formation of an opaque layer by the growing bacterial, thus yielding a clear growth-inhibited area around the sample. This method is commonly used in Europe for screening of antibiotics residues in slaughter animals [63, 64].

4.2 Immunological technique

The immunological techniques work on the principle of antigen-antibody interactions and it is usually very specific and helps in detecting residues from in food producing animals. The enzyme-linked immunosorbent assay (ELISA) is commonly used and detection of antimicrobials is based on enzyme-labeled reagents. ELISA has proven very useful for residual screening in meat especially for tylosin and tetracycline [65, 66]. ELISA's antigen-quantification could take different forms like the direct and indirect sandwich ELISA. Sandwich ELISA works on the principle of recognizing specific antigens that share similar epitopes with other antigens. The indirect sandwich ELISA has the advantage of being highly specific and sensitive. Radioimmunoassay measures the radioactivity of immunological complex using a counter [67].

4.3 Chromatographic method

Liquid chromatography is also useful in the qualitative and quantitative screening of multi-residues in food animals, though its use has rapidly decreased during the last decade [68]. The high-performance liquid chromatography (HPLC) relies on pumps to pass a pressurized liquid solvent containing the sample mixture through a column filled with a solid adsorbent material. Each component in the sample interacts slightly differently with the adsorbent material, causing different flow rates for the different components and leading to the separation of the components as they flow out the column. It has been applied for the detection of antimicrobials in meat, fish and internal organs [69, 70].

Laboratories' use of HPLC has grown very rapidly and has the capacity to analyze multiple residues in a sample within a short time. Also, the equipment is fully automated (injection, elution, washing of column, detection) and controlled with the aid of a computer. Hence, it can be used as a screening technique [68].

Coupling of HPLC with mass spectrometry (MS-MS) has resulted in substantial reduction of analysis time for confirmation in presumed positive samples after initial screening. Such a combination could effectively be used simultaneously for screening and confirmation [71, 72].

4.4 Biosensors

This is a recent and modern approach for detecting veterinary residues in meat and dairy products while ensuring their quality and safety. It has applications for high throughputs within biotechnology. The instrument is made up of biological recognition element (bioreceptor), which recognizes the target antimicrobial residue and a signal transduction element (transducer) which converts the recognition event into a measurable signal [73]. It is usually in close contact and connected to data acquisition and processing systems [74]. The instrument is rapid, highly selective, inexpensive, simple and can be handled by an unskilled personnel [75]. The type of bioreceptor or transducer used forms the basis for classifying biosensors. A bioreceptor can be an organic molecular species (e.g. an antibody, enzyme, protein, or nucleic acid) or a living biological system (e.g. cells, tissues or whole organisms) using biochemical recognition mechanism [76]. Enzymatic biosensors are commonly used for the analysis of herbicides contaminants. Kiran and kale [77] reported an enzyme biosensor that was developed to detect penicillin. However, fewer applications for antibiotic residues and food contaminants have been reported. Cellular biosensors employed for the detection of antibiotic residues such as tetracyclines [78, 79], beta-lactam antibiotics [80, 81]; quinolones [80], chloramphenicol and quinolones [82] have proven to be very effective and fast in detecting of multiple residues simultaneously, within a very short period of time. In transducer-biosensor, common and popular varieties developed for antibiotic residues detection in food producing animals include the mass-based, optical and electrochemical.

5. Possible solution for eliminating antimicrobial residues in meat and meat products

5.1 Promotion of disease resistant livestock breeds

Development and breeding of disease resistant livestock breeds could be a panacea to reduce the use of antimicrobial drugs, antimicrobial residue and antimicrobial resistance in meat and meat products. Some indigenous breeds of cattle, goats and sheep are either tolerant or resistant to specific diseases and parasites, and are also able to withstand very harsh environmental conditions [83]. Evidence has shown that indigenous breeds such as N'Dama cattle, Red Maasai sheep, Meishan pigs, Lohman Brown chickens, Mandarrah chickens and Nguni goat are more resistant to ticks (various species) diseases [84], *Haemonchus contortus* [85] *Sarcocystis miescheriana* [86], *Ascaridia galli* [87], Newcastle disease virus/infectious bursal disease [88] and heart water disease [89], respectively than other breeds. According to Zekarias et al. [90] difference in disease resistance among individuals and breeds are based on immunological system and its interaction with physiological and environmental factors. Alhaji et al. [4] found in their study that antimicrobials are rarely used in local bird flocks, making them likely organic and safe from

antimicrobial residues and resistance. However, most of the indigenous breed are less productive than some imported or exotic breeds and so do not meet producer's needs. It is known in most cases that exotic breeds are easily susceptible diseases and because of this, it is essential to develop breed that are genetically resistant to diseases (either by cross breeding local and exotic animal together), although they may be costly and impossible to achieve in the absence of useful levels of resistance [91]. Selective breeding and management interventions could be a technically feasible approach to manage diseases in livestock.

5.2 Promotion of *in vitro* cultured meat

Another means to reduce antimicrobial residues in meat and meat products is by embracing the production and development of *in vitro* cultured meat when it is commercially available. Basically cultured meat is produced from embryonic stem cells or adult stem cells without slaughtering the animal [92]. It involves culturing of animal muscle cells in a controlled environment (i.e. in a medium that contains nutrients and energy sources required for the division and differentiation of the cells into muscle cells that form into tissue) [93, 94]. The development of cultured meat is projected to compliment conventional meat production and diminish the increasing problems associated with meat including health claims (food-borne illnesses, antimicrobial residues, antimicrobial resistance and animal welfare) [94–97]. The production of *in vitro* culture meat will require the use of fewer livestock to feed the consumers thereby reducing mass production of livestock when commercially available [98]. This in turn will drastically reduce the usage of antimicrobial drugs in prevention and treatment of livestock infection caused by *Salmonella*, *E. coli*, *Campylobacter* and so on. Since meat sold today is raised on factory farms, where animals are fed antimicrobial drugs to keep them disease-free [98], production of *in vitro* cultured meat could be a better option.

5.3 Promotion of ethno-veterinary practices as alternative to veterinary drugs

The role of ethno-veterinary practices in reducing of antibiotic residue and antimicrobial resistance in livestock production is enormous as they are regarded safe and efficacious [99]. They play a significant role in maintaining or restoring animal health in several regions of the world especially in areas where livestock is a main source of income for rural peoples [100]. Ethno-veterinary medicines is often obtained from herbal plants. Recently, there is a greater interest in uses of plants (herbal) due to their accessibility, availability, affordability, efficacy and ease of preparation [100]. Traditional ethno-veterinary medicines have been identified for treatments of small ruminants against ecto- and endo-parasites, gastro-intestinal diseases, viral and bacterial diseases, wounds, sprains and bruises [101]. Furthermore the use of ethno veterinary practices for the treatment of fowl pox in turkey [102], bronchitis [103], hepatotoxicity [104] and foot and mouth disease [104] in ruminants has been established. According to Ranganathan [99], the ethno-veterinary medicine can be advocated to combat issues related to antimicrobial resistance and also minimize the possibility of residues in meat products. Report has shown that the prevalence of antimicrobial resistance was 10–20% lower where antibiotic use was restricted compared to those where it was not [1].

5.4 Other measures for solution

According to Vishnuraj et al. [6], other measures that could be adopted to reduce antimicrobial residues in meat and meat products include (1) reduction of

antimicrobial usage in livestock production (as many developed countries have banned its usage as growth promoters), (2) enforcement of appropriate withdrawal periods of antimicrobial drugs application by government authorities or regulatory bodies before livestock slaughter (3) creation of mass awareness on implication of antimicrobial drugs residues in meat and meat products among consumers, and individual farmer, (4) livestock producer should be educated on farm management, hygiene practices and antimicrobial usages in order to prevent occurrence of antimicrobial residues in meat production and lastly (5) rapid screening methods should be developed for detecting and segregating samples contains above antimicrobial residues before the food products get to consumers. More so, establishment of framework to proper monitoring of drug usage and surveillance of antimicrobial resistance would be of great advantage [105].

6. Conclusion

Findings from this study has shown that the presence of veterinary drug residue in food products is a global health concern as the consequence of using antimicrobial drugs to treat and prevent animal disease extend far beyond the farm. Therefore, the solution to antimicrobial residues will require a coordinated regulatory bodies to monitor the use of antimicrobial drugs to control diseases and also enforce punishment on indiscriminate usage. More so a sensitive, selective and reliable analytical methods to easily detect and monitor antimicrobial residues in meat products should be encouraged.

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Conflict of interest

None declared by the authors.

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References

- [1] WHO. World Health Organization Guidelines on Use of Medically Important Antimicrobials in Food-producing Animals. 2017. Available from: <http://apps.who.int/iris/bitstream/handle/10665/258970/9789241550130-eng.pdf;jsessionid=FD58B9CED3B23E51C59F325F08A89DEF?sequence=1> [Accessed: 15 November 2018]
- [2] Moreno L, Lanusse C. Veterinary drug residues in meat-related edible tissues. In: *New Aspects of Meat Quality*. United Kingdom: Woodhead Publishing Limited; 2017. pp. 581-603. ISBN: 978-0-08-100593-4
- [3] Landoni MF, Albarellos G. The use of antimicrobial agents in broiler chickens. *The Veterinary Journal*. 2015;**205**:21-27
- [4] Alhaji NB, Haruna AE, Muhammada B, Lawan MK, Isol TO. Antimicrobials usage assessments in commercial poultry and local birds in North-Central Nigeria: Associated pathways and factors for resistance emergence and spread. *Preventive Veterinary Medicine*. 2018;**154**:139-147
- [5] Prajwal S, Vasudevan VN, Sathu T, Irshad A, Nayankumar SR. Kuleswan Pame antibiotic residues in food animals: Causes and health effects. *The Pharma Innovation Journal*. 2017;**6**(12):01-04
- [6] Vishnuraj MR, Kandeepan G, Rao KH, Chand S, Kumbhar V. Occurrence, public health hazards and detection methods of antibiotic residues in foods of animal origin: A comprehensive review. *Food and Agriculture*. 2016;**2**:1235458
- [7] Aarestrup F. Sustainable farming: Get pigs off antibiotics. *Nature*. 2012;**486**:465-466. DOI: <http://dx.doi.org/10.1038/486465a>
- [8] Food and Drug Administration (FDA). CVM Updates-CVM Reports on Antimicrobials Sold or Distributed for Foodproducing Animals. Maryland, USA: Silver Spring; 2010
- [9] Van Boeckel TP, Brower C, Gilbert M, Grenfell BT, Levina SA, Robinson TP, et al. Global trends in antimicrobial use in food animals. In: *Proceedings of National Academy of Science*. Washington, DC. 5 May 2015;**112**(18):5649-5654. Available from: www.pnas.org/cgi/doi/10.1073/pnas.1503141112. [Accessed: 15 November 2018]
- [10] Sanz D, Razquin P, Condón S, Juan T, Herraiz B, Mata L. Incidence of antimicrobial residues in meat using a broad spectrum screening strategy. *European Journal of Nutrition and Food Safety*. 2015;**5**(3):156-165
- [11] Federal Ministries of Agriculture, Environment and Health (FMAEH). *Antimicrobial Use and Resistance in Nigeria: Situation Analysis and Recommendations*, 2017. Available from: https://ncdc.gov.ng/themes/common/docs/protocols/56_1510840387 [Accessed: 15 November 2018]
- [12] REGULATION H. Council regulation (EEC) no 2377/90 of 26 June 1990 laying down a community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin. *Official JL*. 1990;**224**:0001-0008
- [13] Nisha AR. Antibiotic residues—A global health hazard. *Veterinary World*. 2008;**1**(12):375-377
- [14] Vragović N, Bažulić D, Njari B. Risk assessment of streptomycin and tetracycline residues in meat and milk on Croatian market. *Food and Chemical Toxicology*. 2011;**49**:352-355

- [15] Woolhouse MEJ et al. Temporal trends in the discovery of human viruses. *Proceedings of the Royal Society B: Biological Sciences*. 2008;**275**:2111-2115
- [16] Perry BD, Grace D, Sones K. Current drivers and future directions of global livestock disease dynamics. 2013;**110**(52):20871-20877
- [17] Page SW, Gautier P. Use of antimicrobial agents in livestock. *Revue Scientifique et Technique (International Office of Epizootics)*. 2012;**31**(1):145-188
- [18] Food and Drug Administration (FDA). 2016 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals. 2017. Available from: <https://www.fda.gov/downloads/.../userfees/animaldruguserfeeactadufa/ucm588085> [Accessed: 15 November 2018]
- [19] Adesokan HK, Agada CA, Adetunji VO, Akanbi IM. Oxytetracycline and penicillin-G residues in cattle slaughtered in South-Western Nigeria: Implications for livestock disease management and public health. *Journal of the South African Veterinary Association*. 2013;**84**(1):945-950. DOI: 10.4102/jsava.v84i1.945
- [20] Cepurnieks G, Rjabova J, Zacs D, Bartkevics V. The development and validation of a rapid method for the determination of antimicrobial agent residues in milk and meat using ultra performance liquid chromatography coupled to quadrupole—Orbitrap mass spectrometry. *Journal of Pharmaceutical and Biomedical Analysis*. 2015;**102**:184-192
- [21] Alvarez-Fernandez E, Cancelo A, Díaz-Vega C, Capita R, Alonso-Calleja C. Antimicrobial resistance in *E. coli* isolates from conventionally and organically reared poultry: A comparison of agar disc diffusion and Sensi Test Gram-negative methods. *Food Control*. 2013;**30**:227-234
- [22] Williams PG. Nutritional composition of red meat. *Nutrition and Dietetics*. 2014;**64**:113-119
- [23] FAO. Food Outlook—Biannual Report on Global Food Markets. 2014. pp. 1-8. Available from: www.fao.org/docrep/019/i3751e/i3751e.pdf [Accessed: 15 October 2018]
- [24] WWF Report. Social, Economic and Environmental Analysis of Soybean and Meat Production in Paraguay. 2016. Available from: www.awsassets.panda.org [Accessed: 19 October 2018]
- [25] OECD/FAO. OECD-FAO Agricultural Outlook, OECD Agriculture Statistics (Database). 2018. <http://dx.doi.org/10.1787/agr-outl-data-en>. [Accessed: 15 November 2018]
- [26] Song JS, Park SJ, Choi JY, Kim JS, Kang MH, Choi BK, et al. Development of analytical method and monitoring of veterinary drug residues in Korean animal products. *Korean Journal for Food Science of Animal Resources*. 2016;**36**:319-325
- [27] Lee MH, Lee HJ, Ryu PD. Public health risks: Chemical and antibiotic residues-review. *Asian-Australasian Journal of Animal Science*. 2001;**14**:402-413
- [28] Lee H-C, Chen C-H, Wei J-T, Chiu HY. Analysis of veterinary drug residue monitoring results for commercial livestock products in Taiwan between 2011 and 2015. *Journal of Food and Drug Analysis*. 2018;**26**:565-571
- [29] Skockova A, Kolackova I, Bogdanovicova K, Karpiskova R. Characteristic and antimicrobial resistance in *Escherichia coli* from retail meats purchased in the Czech Republic. *Food Control*. 2015;**47**:401-406

- [30] Moniri R, Dastehgoli K. Fluoroquinolone-resistant *Escherichia coli* isolated from healthy broilers with previous exposure to fluoroquinolones: Is there a link? *Microbial Ecology in Health and Disease*. 2005;**17**(2):69-74
- [31] Hammerum AM, Heuer OE. Human health hazards from antimicrobial-resistant *Escherichia coli* of animal origin. *Clinical Infectious Diseases*. 2009;**48**:916-921
- [32] Liu CK. Caution with animal drugs to prevent food safety. In: *Veterinarian Newsletter*. Vol. 2. Animal Health Research Institute, Council of Agriculture; 2011. pp. 15-17
- [33] Butaye P, Devriese LA, Haesebrouck F. Differences in antibacterial resistance patterns of enterococcus faecalis and *Enterococcus faecium* strains isolated from farm and pet animals. *Antimicrobial Agents and Chemotherapy*. 2001;**45**:374-1378
- [34] Wegener HC, Aarestrup FM, Jensen LB, Hammerum AM, Bager F. Use of antimicrobial growth promoters in food animals and enterococcus faecium resistance to therapeutic antimicrobial drugs in Europe. *Emerging Infectious Diseases*. 1999;**5**:329-335
- [35] Baynes RD, Dedonder K, Kisell L, Mzyk L, Marmulak T, Smith G, et al. Health concerns and management of select veterinary drug residues. *Food and Chemical Toxicology*. 2016;**88**:112-122
- [36] Lee SY, Kim OY, Yoon SY, Lee DY, Hur SJ. Changes in resistance to and antimicrobial activity of antibiotics during in vitro human. *Digestion*. *Journal of Global Antimicrobial Resistance*. 2018;**15**:277-282
- [37] Dayan AD. Allergy to antimicrobial residues in food: Assessment of the risk to man. *Veterinary Microbiology*. 1993;**35**(34):213-326
- [38] Thong BY, Tan TC. Epidemiology and risk factors for drug allergy. *British Journal of Clinical Pharmacology*. 2011;**71**(5):684-700
- [39] Choquet-Kastylevsky G, Vial T, Descotes J. Allergic adverse reactions to sulfonamides. *Current Allergy and Asthma Reports*. 2002;**2**:16-25
- [40] Darwish WS, Eldaly EA, El-Abbasy MT, Ikenaka Y, Nakayama S. Antibiotic residues in food: The African scenario. *Japanese Journal of Veterinary Research*. 2013;**61**:13-22
- [41] Bendesky A, Menendez D, Ostrosky-Wegman P. Is metronidazole carcinogenic? *Mutation Research*. 2002;**511**(2):133-144
- [42] Vollaard EJ, Clasener HAL. Colonization resistance. *Antimicrobial Agents and Chemotherapy*. 1994;**38**:409-414
- [43] Carman RJ, Van Tassell MS, Wilkins TD. The normal intestinal microflora: Ecology, variability and stability. *Veterinary and Human Toxicology*. 1993;**35**(1):11-14
- [44] Edlund C, Nord CE. Effect of quinolones on intestinal ecology. *Drugs*;**1999**, **58**(2):65-70
- [45] Cerniglia CE, Kotarski S. Approaches in the safety evaluations of veterinary antimicrobial agents in food to determine the effects on the human intestinal microflora. *Journal of Veterinary Pharmacology*. 2005;**28**:3-20
- [46] Cotter PD, Stanton C, Ross RP, Hill C. The impact of antibiotics on the gut microbiota as revealed by high throughput DNA sequencing. *Discovery Medicine*. 2012;**13**:193
- [47] Booth NH, McDonald LE. Toxicology of drug and chemical residues. In: *Veterinary Pharmacology*

and Therapeutics. 6th ed. USA: Iowa State University Press; 1988. pp. 1149-1195

[48] Foster W, Beecroft ML. Chemical exposures and human fertility. In: Infertility Awareness Association of Canada. 2014. Available from: <http://www.cwhn.ca/en>. [Accessed: 15 November 2018]

[49] Aiello SE, Lines PR, Kehn CM. Anthelmintics. In: The Merck Veterinary Manual. 9th ed. Kenilworth, NJ, USA: Merck & Co., Inc.; 2005. pp. 2111-2124

[50] El-Makawy A, Radwan HA, Ghaly IS, El-Raouf AA. Genotoxic, teratological and biochemical effects of anthelmintic drug oxfendazole maximum residue limit (MRL) in male and female mice. *Reproduction, Nutrition, Development*. 2006;**46**:139-156

[51] Horrigan L, Robert SL, Walker P. How sustainable agriculture can address the environmental and human health arms of industrial agriculture. *Environmental Health Perspectives*. 2002;**110**:445-456

[52] Wilson JS, Otsuki T, Majumdar B. Balancing food safety and risk: Do drug residue affect international trade in beef? In: America Agricultural Economics Association Annual Meeting, Montreal, Canada July 2003. pp. 27-30

[53] Wessel JR. Codex committee on pesticide residues 'a plan for improved participation by governments'. *Regulatory Toxicology and Pharmacology*. 1992;**16**(2):126-149

[54] International Agricultural Trade Research Consortium (IATRC). The Role of Product Attributes in the Agricultural Negotiations. St. Paul, MN: University of Minnesota, Department of Applied Economics, Commissioned. 2001. pp. 17

[55] Van den Bogaard AE, Stobbering EE. Epidemiology of resistance to antibiotics. Links between animals and humans. *International Journal of Antimicrobial Agents*. 2000;**14**:327-335

[56] Pena A, Serrano C, Reu C. Antibiotic residues in edible tissues and antibiotic resistance of faecal *Escherichia coli* in pigs from Portugal. *Food Additives and Contaminants*. 2004;**21**:749-755

[57] Guest GB, Paige JC. The magnitude of the tissue residue problem with regard to consumer needs. *Journal of the American Veterinary Medical Association*. 1991;**198**:805-808

[58] Paige JC. Analysis of tissue residues. *FDA Veterinary*. 1994;**1979**(9):4-6

[59] Vermunt AEM, Stadhouders J, Loeffen GJM, Bakker R. Improvements of the tube diffusion method for the detection of antibiotics and sulfonamide in raw milk. *Netherlands Milk and Dairy Journal*. 1993;**47**:31-40

[60] Suhren G, Heeschen W. Detection of inhibitors in milk by microbial tests. A review. *Nahrung*. 1996;**40**:1-7

[61] Cantwell H, O'Keeffe M. Evaluation of the Premi[®] Test and comparison with the one-plate test for the detection of antimicrobials in the kidney. *Food Additives and Contaminants*. 2006;**23**:120-125

[62] Kilnic B, Meyer C, Volker H. Evaluation of the EEC four-plate test and Premi test for screening antibiotic residues in trout (*Salmo trutta*). *International Journal of Food Science and Technology*. 2007;**42**(5):635-628

[63] Nouws JFM, Schothorst M, Ziv G. A critical evaluation of several microbiological test methods for residues of antimicrobial drugs in ruminants. *Archiv für Lebensmittelhygiene*. **30**:4-8

- [64] Bogaerts R, Wolf F. Standardized method for the detection of residues of antibacterial substances in fresh meat. *Fleischwirtsch.* 1980;**60**:672-673
- [65] Mahgoub O, Kadim IT, Ann Mothershaw AI, Zadjali SA, Annamalai K. Use of enzyme-linked immune sorbent assay (ELISA) for detection of antibiotic and anabolic residues in goat and sheep meat. *World Journal of Agricultural Sciences.* 2006;**2**:298-302
- [66] Kadim IT, Mahgoub O, Al-Marzooqi W, Al-Magbaly R, Annamal K, Khalaf S. Enzyme-linked immunosorbent assay for screening antibiotic and hormone residues in broiler chicken meat in Sultanate of Oman. *Journal of Muscle Foods.* 2009;**21**(2):243-254
- [67] Samarajeewa U, Wei CI, Huang TS, Marshall MR. Application of immunoassay in the food industry. *Critical Reviews in Food Science and Nutrition.* 1991;**1991**, **29**:403-434
- [68] Fidel T, Milagro R. Methods for rapid detection of chemical and veterinary drug residues in animal foods. *Trends in Food Science and Technology.* 2006;**17**:482-489
- [69] Cinquina AL, Roberti P, Gianetti L, Longo F, Draisci R, Fagiolo A. Determination of enrofloxacin and its metabolite ciprofloxacin in goat milk by high-performance liquid chromatography with diode-array detection. Optimization and validation. *Journal of Chromatography A.* 2003;**987**:221-226
- [70] Kirbis A, Marinsek J, Flajs VC. Introduction of the HPLC method for the determination of quinolone residues in various muscle tissues. *Biomedical Chromatography.* 2005;**19**:259-265
- [71] Hewitt SA, Kearney M, Currie JW, Young PB, Kennedy DG. Screening and confirmatory strategies for the surveillance of anabolic steroid abuse within Northern Ireland. *Analytica Chimica Acta.* 2002;**473**:99-109
- [72] Thevis M, Opfermann G, Schanzer W. Liquid chromatography/electrospray ionization tandem mass spectrometric screening and confirmation methods for β -agonists in human or equine urine. *Journal of Mass Spectrometry.* 2003;**38**:1197-1206
- [73] Velusamy V, Arshak K, Korostynska O, Olivia K, Adley C. An overview of foodborne pathogen detection: In the perspective of biosensors. *Biotechnology Advances.* 2010;**28**(2):233-254
- [74] Patel PD. Biosensors for measurement of analytes implicated in food safety: A review. *TrAC: Trends in Analytical Chemistry.* 2002;**21**:96-115
- [75] Valerie G. Advances in biosensor development for the screening of antibiotic residues in food products of animal origin—A comprehensive review. *Biosensors and Bioelectronics.* 2017;**90**:363-377
- [76] Vo Dinh T, Cullum B, Fresenius. Biosensors and biochips: Advances in biological and medical diagnostics. *Journal of Analytical Chemistry.* 2000;**366**(6-7):540-551
- [77] Kirian BR, Kale KU. Transformed *E. coli* JM 109 as a biosensor for penicillin. *Indian Journal of Pharmaceutical Sciences.* 2002;**83**(3):205-208
- [78] Bahl MI, Hansen IH, Sorensen SJ. Construction of an extended range whole-cell tetracycline biosensor by use of the tet(M) resistance gene. *FEMS Microbiology Letters.* 2005;**253**(2):201-205
- [79] Virolainen NE, Pikkemaat MG, Elferink JWA, Karp MT. Rapid detection of tetracyclines and their 4-epimer

derivatives from poultry meat with bioluminescent biosensor bacteria. *Journal of Agricultural and Food Chemistry*. 2008;**56**(23):11065-11070

[80] Ben-Yoav H, Elad T, Shlomovits O, Belkin S, Shacham-Diamand Y. Optical modeling of bioluminescence in whole cell biosensors. *Biosensors and Bioelectronics*. 2009;**24**(7):1969-1973

[81] Ferrini AM, Mannoni V, Carpico G, Pellegrini GE. Detection and identification of beta-lactam residues in milk using a hybrid biosensor. *Journal of Agricultural and Food Chemistry*. 2008;**56**:784788

[82] Shapiro E, Baneyx F. Stress-activated bioluminescent *Escherichia coli* sensors for antimicrobial agents detection. *Biotechnology*. 2007;**132**(4):487-493

[83] Mwai O, Hanotte O, Kwon Y, Cho S. African indigenous cattle: Unique genetic resources in a rapidly changing world. *Asian-Australasian Journal of Animal Science*. 2015;**28**(7):911-921

[84] Claxton J, Leperre P. Parasite burdens and host susceptibility of Zebu and N'Dama cattle in village herds in the Gambia. *Veterinary Parasitology*. 1991;**40**(3-4):293-304

[85] Baker RL. Genetic resistance to endoparasites in sheep and goats. A review of genetic resistance to gastrointestinal nematode parasites in sheep and goats in the tropics and evidence for resistance in some sheep and goat breeds in sub-humid coastal Kenya. *Animal Genetic Resources Information*. 1998;**24**:13-30

[86] Reiner G, Eckert J, Peischl T, Bochert S, Jäkel T, Mackenstedt U, et al. Variation in clinical and parasitological traits in Pietran and Meishan pigs infected with *Sarcocystis miescheriana*. *Veterinary Parasitology*. 2002;**106**(2):99-113

[87] Permin A, Ranvig H. Genetic resistance to *Ascaridia galli* infections in chickens. *Veterinary Parasitology*. 2001;**102**(2):101-111

[88] Hassan MK, Afify MA, Aly MM. Genetic resistance of Egyptian chickens to infectious bursal disease and Newcastle disease. *Tropical Animal Health and Production*. 2004;**36**(1):1-9

[89] Irvin AD, McDermott JJ, Perry BD. Epidemiology of ticks and tick-borne diseases in eastern, central and southern Africa. In: *Proceedings of a Workshop Held in Harare*. Nairobi, Kenya: International Livestock Research Institute (ILRI); 1996. pp. 174

[90] Zekarias B, TerHuurne Agnes AHM, Landman Wil JM, Rebel Johanna MJ, Pol Jan MA, Erik G. Immunological basis of differences in disease resistance in the chicken. *Veterinary Research*. 2002;**33**(2):109-125. DOI: 10.1051/vetres:2002001

[91] Cock J, Gitterle T, Salazar M, Rye M. Breeding for disease resistance of Penaeid shrimps. *Aquaculture*. 2009;**286**:1-11

[92] Post MJ. Cultured meat from stem cells: Challenges and prospects. *Meat Science*. 2012;**92**:297-301

[93] Bhat ZF, Kumara S, Fayaz H. In vitro meat production: Challenges and benefits over conventional meat production. *Journal of Integrative Agriculture*. 2015;**2**(14):241-248

[94] Datar I, Betti M. Possibilities for an in vitro meat production system. *Innovative Food Science and Emerging Technologies*. 2010;**11**:13-22

[95] Tuomisto HL. Food security and protein supply-cultured meat a solution? *Annals of Applied Biology*. 2010;**102**:99-104

- [96] Zaraska M. Lab-grown beef taste test: 'Almost' like a burger. Health and Science, The Washington Post. 2013. Available from: www.washingtonpost.com/health-science/lab-grown-beef [Accessed: 5 November 2018]
- [97] Chiles RT. Intertwined ambiguities: Meat, in vitro meat, and the ideological construction of the marketplace. *Journal of Consumer Behaviour*. 2013;**12**:472-482
- [98] Murthy MSS. Meat without slaughter. *Science Reporter*. 2012;**49**(10):56-57. Available from: <http://www.niscair.res.in> [Accessed: 30 November 2018]
- [99] Ranganathan V. Ethno veterinary practices for combating antimicrobial resistance. *International Journal of Science, Environment and Technology*. 2017;**1**(6):840-844
- [100] Wanzala W, Zessin KH, Kyulec NM, Baumann MPO, Mathias E, Hassanali A. Ethnoveterinary medicine: A critical review of its evolution, perception, understanding and the way forward. *Livestock Research for Rural Development*. 2005;**17**(11):1-41
- [101] Piluzza G, Viridis S, Serralutzu F, Bullitta S. Uses of plants, animal and mineral substances in Mediterranean ethno-veterinary practices for the care of small ruminants. *Journal of Ethnopharmacology*. 2015;**168**:87-99
- [102] Basheer Ahamad D, Punniamurthy NSS, Ranganathan V. Pathomorphology and ethno veterinary herbal intervention in an outbreak of Turkey pox. *Indian Journal of Veterinary Pathology*. 2013;**37**(1):18-21
- [103] Pala NA, Negi AK, Todaria NP. Traditional uses of medicinal plants of Pauri, Garhwal, Uttarakhand. *New York Science*. 2010;**3**(6):61-65
- [104] Punniamurthy N, Ranganathan V, Basheer Ahamad D, Sathesh KS. Hepatoprotective activity of *Caralluma umbellata* in chicken. *The Indian Veterinary Journal*. 2014;**91**(12):33-35
- [105] WHO. WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food. 2000. Available from: <http://www.who.int/emc>