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REVIEW

Antibiotic residues in food: the African scenario

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Abstract

Antibiotics are substances either produced naturally by living organisms or synthetically in the laboratory, and they are able to kill or inhibit the growth of microorganisms. Antibiotics are also used as feed additives for the purpose of livestock health maintenance. Antibiotic residues in feedstuffs are currently a problem of some magnitude in different parts of the world, particularly due to associated public health concerns that include hypersensitivity reactions, antibiotic resistance, toxicity, teratogenicity, and carcinogenicity.

In Africa, as in other parts of the world, antibiotic residues in animal-derived foods have been extensively recorded in many African countries; these residues have exceeded the WHO maximum residue levels in many cases.

It has been reported that tetracyclines are the most predominantly prescribed antibiotics in Africa, and of all antibiotic-associated residues they represent 41% of cases, followed by β-lactams at 18%. Great care should be taken to monitor antibiotic cessation periods before the release of animal-derived foods for human consumption. In addition, strict legislation should be implemented in order to minimize the abuse of antibiotics.

Key Words: antibiotics, residues, Africa

Introduction

Antibiotics are substances either produced naturally by living organisms or produced synthetically in the laboratory, and they are able to kill or inhibit the growth of microorganisms. Antibiotics can be classified according to their effects as either bactericidal or bacteriostatic and also according to their range of efficacy as narrow or broad in spectrum.

The use of antibiotics in animals shortly followed their use in humans for the purpose of disease prevention and treatment[17]. Today, antimicrobial drugs are used to control, prevent, and treat infection and to enhance animal growth and feed efficiency[48]. Currently, approximately

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80% of all food-producing animals receive medication for part or most of their lives. The most commonly used antimicrobials in food-producing animals are the β-lactams, tetracyclines, aminoglycosides, lincosamides, macrolides, pleuromutilins, and sulfonamides[25].

The use of antibiotics in food-producing animals may leave residues in foodstuffs of animal origin like meat, milk, and eggs. The occurrence of these residues may be due to any one of the following: a failure to observe the withdrawal periods of each drug, extra-label dosages for animals, contamination of animal feed with the excreta of treated animals, or the use of unlicensed antibiotics[37].

Antibiotic residues in foods of animal origin may be the cause of numerous health concerns in humans. These problems include toxic effects, transfer of antibiotic resistant bacteria to humans, immunopathological effects, carcinogenicity (e.g., sulphamethazine, oxytetracycline, and furazolidone), mutagenicity, nephropathy (e.g., gentamicin), hepatotoxicity, reproductive disorders, bone marrow toxicity (e.g., chloramphenicol), and allergy (e.g., penicillin)[33].

In Africa, in parallel to the incautious use of antibiotics in human medicine, agricultural sectors consume a large portion (50%) of antibiotics in animal farming to treat or to minimize potential outbreaks of diseases or to promote animal health[28]. However, there is no clear regulation controlling antibiotic contamination of feedstuffs in many African countries. Additionally, there is a clear lack of available information about antibiotic residues in animal-derived foods in Africa. Thus, the aim of this review is to document and discuss the African scenario in regard to antibiotic residues in foods, address the public health implications of the effects of these residues, and highlight recommended strategies for controlling this serious problem.

Occurrence of antibiotic residues in foods

The introduction of antibiotics to the veterinary field started soon after the use of antibiotics for the treatment of bacterial diseases in humans. The main use of antibiotics in animal rearing was for the treatment and prevention of diseases. Indeed, antibiotics have been used for the treatment of mastitis, arthritis, respiratory diseases, gastrointestinal infections, and other infectious bacterial diseases[10].

More recently antibiotics have been used for improved growth, especially in broilers and fatteners. Indeed, antibiotics may improve growth rate by the following means: the thinning of mucous membranes in the gut, which facilitates absorption; alteration of gut motility, which enhances assimilation; production of favorable conditions for beneficial gut microbes by destroying harmful bacteria; and partitioning of proteins for muscle growth via cytokine suppression. Antibiotics also favor growth by decreasing the activity of the immune system, reducing the waste of nutrients, and reducing toxin formation. In most cases, however, only young growing animals and poultry are responsive to antibiotic-mediated health maintenance[33]. This approach actually is problematic as these feed additives are usually used without prescription and for very long periods, in both large and small doses, which leads to drug residues entering animal-derived food.

It is a common practice among livestock producers to treat entire groups of livestock, such as birds, fish, or other animals despite there being only a few affected individuals. Such practices unintentionally and unnecessarily expose healthy individuals to antibiotics. Additionally, many livestock producers use subtherapeutic doses of antibiotics to prevent diseases and this of course will lead to antibiotic residues entering the human food chain. Moreover, antibiotics are prescribed inappropriately in cases of viral infection, which do not respond to such drugs.

All licensed antibiotics intended for animal use have clear cessation of use periods, pharmacokinetics and pharmacodynamics. Failure to observe the instructions for antibiotic use can lead to antibiotic residues entering animal-derived foods. Improper maintenance of treatment records or a failure to identify treated animals adequately may lead to their omission of these animals[44]. Residues may also transmit vertically to calves consuming milk from cows receiving antimicrobials[16]. Fecal recycling, where the drug excreted in the feces of treated animals contaminates the feed of untreated animals, can be the cause of traces of certain antimicrobial substances being passed on[26]. Contamination of animal feedstuffs with a variety of compounds may also occur. The significance of this contamination depends on the pharmacodynamics of the compound and the species affected[27,32].

Incidence of antibiotic residues in food in African countries

In many African countries, antibiotics may be used indiscriminately for the treatment of bacterial diseases or they may be used as feed additives for domestic animals and birds. The ongoing threat of antibiotic contamination is one of the biggest challenges to public health that is faced not only by the African people, but also by the human population worldwide[8]. Such residues are spreading rapidly, irrespective of geographical, economical, or legal differences between countries[18].

In one study, ceftazidime residues were recorded in the tissues of rabbits reared in Egypt (Table 1), with the highest concentrations seen in kidney, liver, heart, and muscle tissues[1]. Erythromycin was rapidly passed from blood to milk in experimentally treated lactating ewes[15]. Amoxicillin is commonly used in hen farms in

Table 1. Antibiotic contamination in various foodstuffs consumed in African countries

Country	Antibiotic	Foodstuff	Reference
Egypt	Tetracyclines	Chicken meat	Salama *et al.*, 2011
		Bovine carcasses	Morshdy *et al.*, 2013
	β-lactams	Eggs	Khattab *et al.*, 2010
	Cephalosporines	Rabbit meat	AbdEl-Aty *et al.*, 2001
		Rabbit liver	
		Rabbit kidney	
	Macrolides	Milk	Goudah *et al.*, 2007
Sudan	Quinolones	Animal-derived foods	El-tayeb *et al.*, 2012
	Tetracyclines	,,	
Kenya	Tetracyclines	Beef, liver & kidney	Muriuki *et al.*, 2001
	β-lactams	milk	Shitandi and Sternjo, 2001
Ethiopia	Tetracyclines	Meat & edible tissues	Myllyniemi *et al.*, 2000
Tanzania	Tetracyclines	Milk	Kurwijila *et al.*, 2006
		Eggs	Nonga *et al.*, 2010
	Chloramphenicol	,,	
Nigeria	Tetracyclines	Meat	Olufemi and Agboola, 2009
		Eggs	Ezenduka *et al.*, 2011
	Nitrofurans	Animal-derived foods	
	Clhoramphenicol	Eggs	Omeiza *et al.*, 2012
	β-lactams	Cattle meats	Ibrahim *et al.*, 2010
Ghana	Tetracyclines	Milk	Addo *et al.*, 2011
South Africa	Tetracyclines	Milk	Bester and Lombard, 1979

Egypt for the prevention and control of many bacterial diseases. The cessation of use time of amoxicillin is seven days. A study was undertaken to detect amoxicillin residues in laying chickens and commercial eggs. The effects of cooking and storage on amoxicillin contamination in the eggs were also assessed. Levels were detected in both egg yolks and egg whites for six successive days after last exposure to the drugs (Table 1). It was found that amoxicillin residues remained until the seventh day after drug administration in eggs stored at room temperature and at 4°C. Amoxicillin residues were not affected after these eggs were boiled for ten minutes[22].

The incidence of tetracycline residues (e.g., oxytetracycline, tetracycline, chlorotetracycline, and doxycycline) in fresh chicken samples (meat and liver) collected over the course of one year from retail shops in Cairo was also recorded (Table 1). The results revealed that 66 samples (44%) contained tetracycline residues including 21 breast (42%), 19 thigh (38%), and 26 liver (52%) samples. The corresponding ranges of contamination were 124–5812, 107–6010, and 103–8148 $\mu g\ kg^{-1}$. A respective 8%, 7%, and 13% of samples of breast, thigh, and liver had tetracycline residues above the maximum residue limits (Table 2). Liver samples had a higher incidence and content than those from breast or thigh[41]. Oxytetracycline residues were examined in 600 samples (made up of 200 samples from muscle, liver, and kidney) collected randomly from bovine carcasses slaughtered at the Mansoura Abattoir (Dakahlia Province, Egypt). Two percent of samples tested positive for residues. Oxytetracycline residues exceeded the maximum limits (Tables 1 & 2) in 1.3% of the samples examined[30].

In Sudan, the most commonly used antibiotics by farmers in Khartoum are quinolones and tetracyclines. The majority of farmers use antibiotics for prevention and control of disease; only 5% of farmers use antibiotics for livestock health maintenance[12].

In Kenya, tetracyclines, sulfonamides and trimethoprim, nitrofurans, aminoglycosides, β-lactams, and quinolones are the most commonly used drugs in food-producing animals (Table 1). A total of 250 beef samples were collected from five slaughterhouses in and around the city of Nairobi. Out of the 250 samples that were analyzed for tetracycline residues, 114 (45.6%) had detectable tetracycline residues. Of those 114 samples, 60 (24%) were from liver, 35 (14%) from kidney, and 19 (7.6%) from muscle. The mean tetracycline levels of samples from the five slaughterhouses in the study were as follows: Athi River, 1,046 μg/kg; Dandora, 594 μg/kg; Ngong, 701 μg/kg; Kiserian, 524 μg/kg; and Dagoretti, 640 μg/kg. Of the 250 samples analyzed 110 (44%) had oxytetracyclines while 4 (1.6%) had chlortetracyclines. The mean levels of the detected tetracyclines were higher than the recommended maximum levels in edible tissues (Table 2)[31,50]. In milk, a higher prevalence of antimicrobial residues was also reported. For example, 11% of raw bulk milk samples sold in Nakuru was found to have penicillin-G residues[43] and 9–16% of the marketed milk in rural and urban households in the Dagoritti division, Nairobi, contained higher levels of antibiotics[11,20]. Additionally, there was a steady increase in the

Table 2. Maximum residual limits (MRLs) of tetracyclines in animal-derived foods according to the WHO, 1999

Antibiotic	Tissue	MRLs
Tetracyclines (Oxytetracycline, tetracycline, chlortetracyclines)	Muscle	200 μg/kg
	Liver	600 μg/kg
	Kidney	1200 μg/kg
	Milk	100 μg/kg
	Eggs	400 μg/kg

consumption of quinolones, which was first seen in 1998[29].

In Tanzania, antimicrobial residues were detected in 36% of marketed milk samples from milk supply chains in and around Mwanza and Dar es Salaam during 1999 and 2000[24]. The occurrence of antibiotic residues in commercial chicken eggs was determined in the Morogoro municipality between January and February 2007. All eggs examined tested positive for antibiotic residues (Table 2). The common drugs detected were oxytetracycline, chlortetracyclines, chloramphenicol, doxycycline, and flumequine[34].

In Ethiopia, a cross-sectional study was conducted from October 2006 to May 2007 to estimate the proportion of tetracycline levels in beef; the study focused on the Addis Ababa, Debre Zeit, and Nazareth slaughterhouses. Out of the total 384 samples analyzed for tetracycline residues, 71.3% had detectable oxytetracycline levels. Among the meat samples collected from the Addis Ababa, Debre Zeit, and Nazareth slaughterhouses, 93.8%, 37.5%, and 82.1% tested positive for oxytetracycline. The mean levels of oxytetracycline in muscle from the three slaughterhouses were as follows: Addis Ababa, 108.34 μg/kg; Nazareth, 64.85 μg/kg; and Debre Zeit, 15.916 μg/kg. Regarding kidney samples, oxytetracycline levels were found to be 99.02 μg/kg in Addis Ababa, 109.35 μg/kg in Nazareth, and 112.53 μg/kg in Debre Zeit. About 48% of the edible tissues had oxytetracycline levels above the recommended maximum limits (Table 2)[32,50].

In Nigeria, a study was designed to determine the prevalence of antibiotics in eggs from poultry farms and retail outlets in Enugu State. Eggs from 25 selected commercial farms and ten retail outlets were screened for the occurrence of antibiotic residues. All 25 farms surveyed used oxytetracycline (Table 1). Eggs from nine of the surveyed farms tested positive for antimicrobial residues and three of the ten outlets also tested positive for antimicrobial residues. Drugs like nitrofurans, which have been banned in food animals, are still very much in use in Enugu State, Nigeria[13]. Chloramphenicol, despite being banned in food-producing animals, is still used in poultry farms in Nigeria. In a survey of chloramphenicol use in poultry farms in Kaduna state, 21 farm authorities (20.0%) admitted the use of chloramphenicol in both human and veterinary preparations, while 15 (62.5%) admitted to the use of a chloramphenicol preparation intended for humans. The presence of antimicrobials was confirmed in eight out of 144 pooled egg samples (10 eggs per sample). The only positive chloramphenicol sample was recorded on a farm that used a human chloramphenicol preparation (Table 1)[36]. Similar reports from different parts of the world, although experimental, have demonstrated the presence and persistence of chloramphenicol residues in tissue from poultry and cattle.[4,23,40]. Meat and other edible tissue from cattle slaughtered in the Akure metropolitan abattoir were analyzed from January to June 2008 for oxytetracycline residues. Out of a total of 180 beef samples analyzed in this study, 98 (54.44%) had detectable levels of oxytetracycline of which 62 (34.44%) were contaminated to levels considered violative by the WHO/FAO (Table 2)[35,50]. In another report, a microbiological screening was performed for 50 cattle slaughtered in the Sokoto metropolitan abattoir, Nigeria, in order to detect antibiotic residues in meat. A total of 44% of the slaughtered cattle tested positive. Penicillin was the drug with the highest rate of occurrence (14%) followed by tetracycline (8%) and streptomycin (4%) in the samples in question[19].

In Ghana, a report showed that 35% of the raw milk marketed in two major cities, Accra and Kumasi, were contaminated with antibiotics[5]. Additionally, 3.1% of the raw milk samples contained antibiotic levels above the European Union maximum residue limit. The antimicrobials detected included β-lactams, sulphonamides, aminoglycosides, tetracyclines, and macrolides[3].

In South Africa, a survey was done in 1977/78 to investigate the incidence of antibiotic contamination in milk marketed in the markets of Pretoria. In milk from 1081 cattle herds, 60 tankers, and 112 pasteurized batches, antibiotics were found in 2.13% of the herd samples, 11.7% of the tanker samples, and 2.1% of the pasteurized samples[6)].

In the literature discussed above, it is clear that antibiotic residues in animal-derived foods are frequently recorded in several African countries (Table 1). These residues exceeded the WHO limits (Table 2) in many cases. Tetracyclines are highly predominant antibiotics, and represent 41 % of all antibiotic contaminants, followed by β-lactams at 18% (Fig. 1). Great care should be taken to observe the antibiotic cessation of use periods before the production of animal-derived foods intended for human consumption.

The public health importance of antibiotic residues in foods

In many cases the long-term effects of antibiotics on human health are not known, but they can, for example, provoke strong allergic reactions in sensitive people. An allergic reaction may be triggered by antimicrobial residues in a previously sensitized individual. In relation to primary sensitization, it is unlikely that residues could contribute to the overall immune response in view of the very low concentrations that are likely to be encountered. The duration of exposure is also short[9,46)]. Despite their generally non-toxic nature, β-lactams appear to be responsible for most of the reported human allergic reactions to antimicrobials[14,45,49)]. Aminoglycosides, sulphonamides, and tetracyclines may also cause allergic reactions[38)]. Certain macrolides may in exceptional cases be responsible for liver injury caused by a specific allergic response to macrolide metabolite-modified hepatic cells[9)]. However, only a few cases of hypersensitivity have been reported as a result of exposure to residues in meat. Anaphylactic reactions to penicillin in pork and beef have been described[21,39)]. In one case, anaphylaxis was possibly caused by streptomycin residues[47)]. Angioneurotic edema and tightness in the chest may also be caused by penicillin residues in meat[42)].

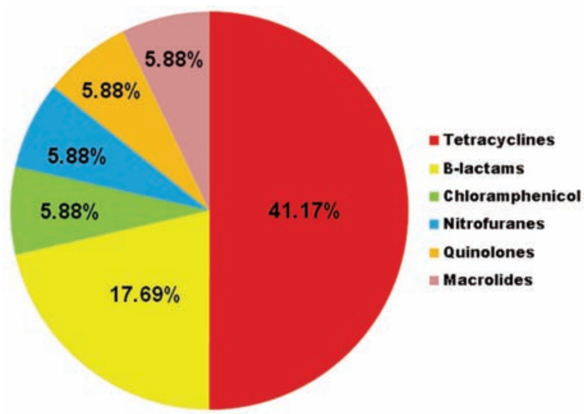

Fig. 1. Distribution of antibiotic residues in African countries.

Antibiotics can encourage the spread of antibiotic resistance in bacteria, making treatment of human infection more difficult. For this reason it has been recommended that antibiotics used in human medicine should not be used in animals. Widespread use of antimicrobials for disease control and health maintenance in animals has been paralleled by an increase in bacterial resistance in those animals. Resistant bacteria then spread among groups of animals, including fish, or to the local environment (i.e., local soil, air, and water) through the spreading of manure or through contaminated foods to humans. Although correct cooking procedure kills bacteria, contamination can occur through improper handling before cooking. Many of the antimicrobial-resistant *E. coli* strains that cause urinary tract and bloodstream infections in humans appear likely to have originated from contaminated retail meat[7)].

Antibiotic residues in milk that is used to produce fermented products can interfere with the fermentation process by affecting desired lactic acid bacteria. Normally this is just a technical problem resulting in financial loss, but, when it occurs, pathogens present in the milk may grow and pose a health hazard later. For these reasons many countries have regulations prohibiting the sale of milk from cows being treated for mastitis, and milk is routinely tested for the presence of antibiotic residues[33].

Disruption of normal human flora in the intestine is another harmful effect of drug residues in human food. The bacteria that usually live in the intestine act as a barrier to prevent incoming pathogenic bacteria from becoming established and causing disease. Antibiotics might reduce total numbers of these benign bacteria or selectively kill some important species[32].

Recommendations for the reduction of antibiotic contamination in food in African countries

There is no doubt that neither humans nor animals can live without antibiotics as they are some of the most effective antimicrobial treatments. However, at the same time, the misuse of antibiotics may result in the aforementioned health hazards. Thus, the reduction of antibiotic use constitutes a challenge for the world. In order to achieve such a reduction, the following ten steps should possibly be considered with regard to all antibiotics:

- The effective prevention of infectious diseases and the adoption of strict hygiene standards and rearing skills may reduce our need for antibiotics, particularly in the veterinary field.
- The use of alternatives to antibiotics, such as plant-derived antimicrobial substances and probiotics, may represent a promising option; vaccination against some bacterial diseases may be of great value in the near future.
- The reduction of unnecessary antibiotic use in animals in captivity should be pursued, as should antibiotic use for the treatment of viral disease in animals; the reduction of prophylactic antibiotic use should also be considered.
- Strict national legislation must be passed around the world to avoid the unnecessary use of antibiotics. In 2006, the European Union banned the use of antibiotics for the purpose of livestock health maintenance[7].
- National monitoring of antibiotic residues in foods and updating of the maximum permissible limits of these residues for each country should be undertaken. In Table 2, we state the maximum limits on commonly observed antibiotic residues in foodstuffs.
- Antibiotics use in feed additives should be ceased.
- Avoid using antibiotics in the veterinary field without a veterinarian's prescription (in some African countries veterinarian or even human medical formulas are sold in supermarkets).
- Strict observation of antibiotic cessation times should be made; the avoidance of antibiotics lacking clearly documented pharmacokinetic and pharmacodynamic properties must be considered.
- The heat treatment of meat, milk, and eggs may inactivate antibiotic contaminants in feedstuffs.
- The freezing of animal-derived foods may also contribute to the reduction of some antibiotic contamination.

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