## ANTIMICROBIAL RESIDUE IN FOOD AND ITS PUBLIC HEALTH HAZARD: A REVIEW



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# ANTIMICROBIAL RESIDUE IN FOOD AND ITS PUBLIC HEALTH HAZARD: A REVIEW



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### Abstract

Antibiotics are life saving drugs for both human and animal health. But indiscriminate application of antibiotics in food animal might result in deposition of residues in meat, milk and eggs which are not permitted in food intended for human consumption. Although use of antibiotics is necessary in treatment of animal diseases, a withdrawal period must be observed until the residues are negligible or no longer detected. Concern over antibiotic residues in food of animal origin occurs in two ways; one is production of direct toxicity in human, second is whether the low levels of antibiotic exposure would result in alteration of microflora, cause disease and the possible development of resistant strains which cause failure of antibiotic therapy in clinical situations. A withdrawal period is established to safeguard human from exposure of antibiotic added food. Heavy responsibility is placed on the veterinarian and livestock producer to observe the period for a withdrawal of a drug prior to slaughter to assure that illegal concentration of drug residue in meat, milk and egg do not occur. But their indiscriminate use will produce toxicity in consumers. In this report we reviewed different published articles and discussed about different kinds of commonly used antibiotics in Bangladesh, their mode of action, uses, withdrawal period and also antimicrobial residue, Maximum Residue Limit (MRL) for veterinary residues, prevalence of antimicrobial residue, treatment effects of antimicrobial residue, acceptable daily intake and public health importance of antimicrobial residue in livestock and poultry.

Keywords: Antibiotic, Antimicrobial Residues, Health Hazard, Drug, Treatment, Withholding period

## **1. Introduction**

Antimicrobials 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 at minimum concentration without causing any harm to host cells (Goodman et al., 1985; Harrison and Svec, 1998). These drugs are not only used for prevention and treatment of diseases, but also used for enhancement of growth and food efficiency especially in food producing animals. Nearly 80% of all food producing animals receives antimicrobials partly or throughout their lives as medication or as growth promoters mostly in developing countries of the world (Lee et al.,2001). Antimicrobials are inclusive of anti-bacterials, anti-virals, anti-fungals, antiprotozoals, coccidiostatic, and antimycotics. On the other hand "Antimicrobial residue" is the small amount of an antimicrobial drug or its breakdown product (s) that remains in or on an agricultural product following treatment with that antimicrobial. Indiscriminate and overuse of antimicrobials could leave high concentrations of residues in edible tissues and tissue by-products. These residues cause antimicrobial resistance and create many harmful effects on human health. Indiscriminate and irrational use of antibiotics in livestock without following withdrawal period may result in unexpected residues in food supplies and could cause serious health hazards to consumers.

## 2. Materials and methods

The information in this report was gathered after reviewing different scientific articles published in different peer reviewed journals, magazines, proceedings; and internet resources. All the articles were collected from different data bases, such as - PubMed, Scopus, and Google Scholar.

## 3. What is Antibiotic?

The term antibiotic was first used in America in the 1700s and described as a compound that killed micro-organisms. Sir Alexander Fleming, a Scottish biologist, defined new horizons for modern antibiotics with his discoveries of enzyme lysozyme (1921) and the antibiotic substance penicillin (1928). The discovery of penicillin from the fungus Penicillium helped treating several bacterial infections such as, syphilis, gangrene and tuberculosis. He also contributed immensely

towards medical sciences with writings on various topics of bacteriology, immunology and chemotherapy.

Antibiotics are drugs of natural or synthetic origin that have the capacity to kill or to inhibit the growth of microorganisms (FAO, 2005). Any chemical substance produced by or derived from one organism that has the capacity to dilute solutions to destroy or inhibit the growth of other organisms. Usually the product of bacteria or fungi, often chemically modified (semi-synthetic antibiotics) that is used to treat infectious diseases of humans or domestic animals (chemical dictionary of science and technology).

#### 3.1. Classification of antimicrobials

Antimicrobials are classified in various ways. According to their chemical structure, each class of antimicrobials is characterized by a typical core structure, and the various members of the class are differentiated by the addition or removal of secondary chemical structures from the core structures (Kennedy et al., 1998; Guardabassi and Dalsgaard, 2004). They can be classified as broad and narrow spectrum, depending on the range of bacterial species against which they are active, or as bacteriostatic or bactericidal on the basis of their mechanism of action. An antimicrobial that exhibits a large dilution difference between inhibitory and cidal effects is considered to be a bacteriostatic drug, whereas an antimicrobial that kills the bacterium at or near the same drug concentration that inhibits its growth is considered to be a bactericidal drug (Prescott, 2000a; Prescott and Walker, 2000b; Mitchell et al.y 1998). Classification of antimicrobials based on mode of action:

- I. Inhibition of cell wall synthesis (3-lactam antibiotics: e.g., penicillin, cephalosporin etc);
- II. Damage to cell membrane function (Polyene antibiotics: e.g., amphotericin, nystatin etc);
- III. Inhibition of nucleic acid synthesis or function (e.g., ciprofloxacin, enrofloxacin etc);
- IV. Inhibition of protein synthesis (Aminoglycosides e.g., streptomycin, tetracycline); and
- V. Inhibition of folic acid synthesis (e.g., sulphonamide) (Prescott, 2000a; Prescott and Walker, 2000b).

# 3.2. Purposes and uses of antimicrobials and other drugs in Livestock and poultry

Globally antimicrobials are commonly used for the treatment, prevention of infectious diseases and for promotion of growth in food-producing livestock, poultry and fish since their discovery (Donoghue, 2003) and now-a-days represent as an extremely important tool in the efficient production of animal products such as meat and eggs (Phillips, 2007). However, many industrial based livestock producing countries for example, India, China and South Africa have been using antimicrobials in a limited scale (Sarmah et al., 2006). Like other developing countries, farmers in Bangladesh also use antimicrobials widely for different purposes in livestock and poultry. Antimicrobials such as ceftiofur are reported to use in freshly hatched chicks to prevent E. coli septicemia (Hasan et al., 2011). In addition, commonly used antimicrobials in poultry production belong to aminoglycosides, tetracyclines, P-lactams, fluroquinolones, macrolides, polypeptides, amphenicols, sulphonamides and trimethoprim (Personal communication to consulting veterinarians in Bangladesh).

In poultry, growth promoters, such as bacitracin, virginiamycin and avoparcin are used to control Clostridium perfringens infections, which are potentially fatal, in addition to improving feed conversion efficiency. Moreover, vitamins, minerals, and amino acids are required in small quantities in the diet for both livestock and human for various metabolic functions to maintain health and promotion of growth.

#### 3.3. Consequences of antimicrobial uses

#### **3.3.1.** Development of antimicrobial resistance

Indiscriminate uses of antimicrobials for different purposes have been reported to cause antimicrobial resistance against different poultry diseases caused by bacteria. However, the rate of resistance varied according to locations and trends of using of antimicrobials in different purposes (Enabulele et al., 2010). Antimicrobial resistance has been recognized as a global health problem. It has now been escalated by major world health organizations to one of the top health challenges facing the twenty-first century (FDA, 2000; CDC, 2010).

The use of antimicrobials in raising food animals has contributed significantly to the global pool of antimicrobial resistant organisms. Antimicrobial resistance in zoonotic enteropathogens including *Salmonella* spp., *Escherichia coli*, and Enterococci in food animals is of special concern to human health because these bacteria are likely to transfer from the food chain to humans (Endtz et al., 1991). The emergence of multi drug resistant bacteria has increased the

need for new antimicrobials or modifications of older antimicrobials (Tollefson and Miller, 2000).

The use of antimicrobials in poultry leads to resistant organisms within the chickens themselves and throughout the production environment. Resistant strains of many organisms, including Staphylococcus, Streptococcus, Clostridium, Pseudomonas, and Aeromonas, have been isolated from these sources (Bass et al., 1999). Resistant *E. coli* are frequently isolated from live chickens and strains with multiple resistance to tetracycline, streptomycin, sulfonamides, gentamicin, fluroquinolones, and virtually all other antibiotics, have been isolated (Blanco et al. 1997). Some of its causes are widely accepted, for example, the inappropriate and overuse of antibiotics for nonbacterial infections such as colds and other viral infections and inadequate antibiotic use in the clinical arena (Levy, 2002). This practice is reported to have caused high resistance to antibiotics by pathogenic micro-organisms in poultry (Sprum and Sunde, 2001).

Single, double and multi-antimicrobial resistances have been reported against bacterial pathogens isolated from broiler chickens in India, Pakistan, Nepal and Bhutan. The common resistant antimicrobials in those studies were streptomycin, tetracycline, gentamicin, ampicillin and nalidixic acid. Similar findings have been observed in many earlier studies in poultry in Bangladesh (Akter et al.y 2007; Ferdous et al., 2013). In Bangladesh antimicrobial agents are readily available to people in local drug stores without prescriptions by registered veterinarians (Kwaga and Adesiyun, 1984 and Hasan et al., 2011). This malpractice of choosing drugs by non veterinarians increases the prevalence of antimicrobial resistance. Available locally produced drugs with the cheap price rate such as ampicillin, amoxicillin, erythromycin, quinolone, neomycin, kanamycin, pefloxacin and sulfamethoxazole could encourage to use them more commonly than the older drugs and therefore drugs become resistant which is evident in poultry farms of India, Bhutan and Brazil (Hart and Kariuki, 1998; Prakash et al., 2005; Dahal, 2007; Haung et a 1 2009 and Eliana et al., 2012). A detailed description of development of antimicrobial resistance is given in Table 1.

Antimicrobial type	Mode of action	Resistant Method
beta-lactam antibiotics:	Inhibit cell wall synthesis	Change their outer membrane
Penicillin, ampicillin,		structure to prevent entrance of
cephalosporine.		the drug.
		• Modify the enzyme so that the

Table 1: Developing of resistance of antimicrobials against pathogens

		<ul> <li>drug no longer binds.</li> <li>Synthesize P-lactamases that cleave the functional lactam ring of the drug.</li> <li>Genes for lactamases are often carried on R-plasmids.</li> </ul>
Aminoglycoside: Gentamycin, kanamycin, neomycin, streptomycin etc. Macrolids: Azithromycin, erythromycin, telirheomycin etc. Tetracyclines: Doxycycline, tetracycline etc	Inhibit protein synthesis	<ul> <li>Uptake of these drugs is energy dependent, so anaerobic bacteria with less ATP available are less susceptible; aerobic bacteria alter membrane pores to prevent uptake or synthesize enzymes that alter or degrade the drug once it enters; rarely bacteria alter the binding site on the ribosome; some bacteria make biofilms when exposed to the drugs.</li> <li>Develops via changes in ribosomal RNA that prevents drugs from binding, or via R-plasmid genes coding for the production of macrolide digesting enzymes: resistance genes are same as those of lincosomides. Bacteria may:</li> <li>Alter gene for pores in the outer membrane; new pore prevents drug from entering cell.</li> <li>Alter binding site on the ribosome to allow tRNA to bind even in presence of drug.</li> <li>Actively pump drug from cell.</li> </ul>
Fluoroquinolones: Ciprofloxacin, moxifloxacin, cinofloxacin etc.	Inhibit nucleic acid synthesis	Ciprofloxacin, moxifloxacin, cinofloxacin etc. Inhibit nucleic acid synthesis • Result from chromosomal mutations that lower affinity for drug, reduce its uptake, or protect gyrase from drug.
Sulfonamides: Sulfadiazine, sulfadoxine, sulfanilamide etc.	Block second metabolic steps in the formation of folic acid from para amino butyric acid (PABA).	• Pseudomonas is naturally resistant due to permeability barriers; cells that require folic acid as a vitamin are also naturally resistant; chromosomal mutations result in lowered affinity for the drugs.

## 4. Antimicrobial residue

The term "Antimicrobial residue" is the small amount of an antimicrobial drug or its breakdown product (s) that remains in or on an agricultural product following treatment with that antimicrobial. Indiscriminate and overuse of antimicrobials could leave high concentrations of residues in edible tissues and tissue by-products (Botsoglou and Fletouris, 2001). The most common causes for the persistence of antimicrobial residues in different organs of poultry are overdosing and violations of withdrawal periods (Pena et al., 2007). Veterinarians in Bangladesh usually do not advice farmers to follow drug withdrawal period for food producing animals and therefore farmers have no knowledge about persistence of drug residues in poultry products which can easily enter into human bodies and become drug resistant against human pathogens (Apata, 2009) and cause other problems such as allergic reactions, cancer etc (Botsoglou and Fletouris, 2001; Donoghue, 2003; Companyo et al., 2009).

## 4.1. Drug withdrawal period

The term "Drug withdrawal period" is often used more broadly to describe the time needed after drug administration to any food animal where drug residue may be found in marketed meats, eggs, organs, or other edible products (Eiichi et al., 2006). Until the withdrawal period has elapsed, the animal or its products must not be used for human consumption. Following table shows the withdrawal period of different antibiotics.

Antimicrobial type	Withdrawal period (days)
Oxytetracycline	7
Ciprofloxacin	6
Amoxicillin	5
Trimethoprim	10
Sulphaquinoxaline	10
Sulphachloropyrazine	5
Sulphadimethoxine	5

 Table 2: Withdrawal periods of different antimicrobials in poultry

(Source: Rana, 1988; Maqbool, 1988; Calnek et al, 1991; Nawaz et al, 1996;; Mumtaz et al.2000)

The occurrence of antimicrobial residues may be due to the failure to observe the withdrawal periods of antimicrobial drugs. To ensure that drug residues have declined to a safe concentration

following the use of drugs in animals, a specified period of drug withdrawal must be observed prior to providing any products for human consumption.

#### 4.2. Prevalence of antimicrobial residues

Estimation of the prevalence of antimicrobial residues in livestock and poultry products has been documented in many different countries of the world and overall prevalence estimates include 14% for penicillin, 8-52% for tetracycline, 28% for oxytetracycline, 4% for streptomycin, 12.5-50% for sulphonamide, 28% for sulphadiazine in poultry products (Diezet et al., 2002; Salem, 2004; Reyes-Herrera et al.v 2005; Shareef et al., 2009). In another study, ciprofloxacin was reported as highest in proportion (6.7%) followed by oxytetracycline (4.2%), amoxicillin (2.5%) and sulfonamides (2.5%), respectively. Some non-systematic studies in Bangladesh estimated prevalence of antimicrobial residues as follows: 37.5% for tetracycline in liver samples of poultry followed by 7.5% for ciprofloxacin and 5% for sulphonamide (Mahmud, 2012; Karim, 2013).

#### 4.3. Concentration of antimicrobial residues

Concentration levels of antimicrobial residues in livestock and poultry products has also been studied worldwide including Bangladesh, and generally there is evidence that concentrations of amoxicillin (50 ng/kg), ampicillin (50 Mg/kg), tetracycline (100-148 ng/kg), sulphonamides (100 ng/kg) and gentamicin (750 ng/kg) routinely exceed upper threshold limits in muscle tissues of poultry (EC, 1998; Diez et al., 2002; Salem, 2004 Hossain et al, 2011; Karim, 2013). However, the cited studies in Bangladesh were cross-sectional and non-systematic studies to quantify concentration of antimicrobial residues; however this investigation was designed as controlled broiler farm setting to assess antimicrobial residues in broiler chicken products for the first time in Bangladesh. Acceptable limits of different antibiotics are shown in Table 3.

Antimicrobial type	Minimum (microgram/kg)	Maximum(microgram/kg)
Amoxicillin	5	40
Tetracycline	15	100
Oxytetracycline	15	100

Table 3: Acceptable limits of antimicrobial residues in livestock and poultry products

Chlortetracycline	15	100
Sulphonamide	25	100
Trimethoprim	8	50
Erythromycin	12	40
Quinolones	47	147

#### 4.4. Treatment effects on antimicrobial residues

Different heat stabilities of antimicrobials between drug classes, between temperature levels, and among the same classes of drugs were studied. Ranking of heat stability by antimicrobial classes at 121°C was the highest for sulphonamide, followed by lincomycin, colistin, tetracyclines and B-lactams while at 100°C sulphonamides equaled lincomycin and was greater than colistin but variability was observed in different tetracyclines and B-lactams. Enrorofloxacin residue determined from 15 samples of chicken remained stable at 100°C for 3 hours (Lolo et al., 2006). Javadi et al. (2009) analyzed that the enrofloxacin residue using microbial inhibition method is reduced in concentration after different cooking process. Sulfamethoxazole, sulfamonomethonine and sulfaquinonaline residues except sulfadiazine residue detected in the muscle of chickens roasted at 170°C for 12 minutes reduced the concentration from 100ng/kg to 25<sup>g</sup>/kg (Furusawa and Hanabusa, 2002).

Stable	Partially stable	Labile
Ciprofloxacin	Amoxillin	Amoxicillin and
		clavulanic acid
Gentamicin	Ampicillin	Cefixime
Norfloxacin	Nitrofurantoin	Ceftriaxone
Trimethoprim	Penicillin G	Cefuroxime
Sulfamethoxazole and	Polymyxin B	Doxycycline
Trimethoprim		
Nalidixic acid	Ampicillin and sulbactum	Erythomycin
Clindamycin	Rafampicin	Tetracycline

Table 4: Heat stability of antimicrobials after autoclaving at 121°C for 15 minutes

(Source: Furusawa and Hanabusa, 2002; Lolo et al.9 2006; avadi et al.9 2009)

Different treatment strategies have potential effects in reducing the prevalence and concentration of antimicrobial residues in animal and poultry products. Some studies in limited scale have been conducted to examine the cooking effects on reducing antimicrobial residues in poultry meat and meat by-products in Chittagong, Bangladesh (Hossain et al. 2011; Mahmud, 2012; Karim, 2013).

#### 4.5. Harmful effects of antimicrobial residues

Antibiotic residues in foods of animal and bird origin might cause problems for several reasons. In addition to toxic effects, effects on intestinal micro-biota and the immune system are important (Gorbach, 1993; Waltner-Toews and McEwen, 1994; Perrin-Guyomard et al., 2001). Microbiological endpoints were considered more valid and sensitive in the safety evaluation of antimicrobial residues in production animals than standard toxicological endpoints (Boisseau, 1993).

#### 4.5.1. Effects on human gut microbiota

The microbiota in the human gastrointestinal tract form an extremely complex, yet relatively stable, ecological community, containing more than 400 bacterial species (Carman et al., 1993). The concentration of anaerobic microbiota is 1011-1012 CFU g-1 facces, and the concentration of aerobic microbiota much lower and less than 0.1% of the normal microbiota consists of aerobes (Vollard and Cleaner, 1994). In addition to the resident dominant anaerobic microbiota, the microbiota consists of a subdominant microbiota, a resident minority microbiota and a variable microbiota composed of bacteria which might be present for a variable period of time (Boisseau, 1993). Colonisation resistance meant the natural defence by normal microbiota against colonization and translocation by exogenous potentially pathogenic microbes or against the overgrowth of indigenous opportunisms (van der Waaij et al., 1971; Barza etal., 1987, Corpet, 1993).

Administration of antimicrobial agents might cause disturbances in these functions (Nord and Edlund, 1990). To what extent disturbances in the ecological balance between host and microorganisms occur depends on the spectrum of the antimicrobial agent, the dose, pharmacokinetic and pharmacodynamic properties, and in-vivo inactivation of the agent (Sullivan et al., 2001). Four microbiological endpoints have been identified that could be of public health concern: modification of the metabolic activity of microbiota, changes in bacterial

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populations, selection of resistant bacteria, and perturbation of the barrier effect (Boisseau, 1993; Gorbach, 1993; Sundlof et al., 2000; Perrin- Guyomard et al., 2001).

In cases of reduced colonization resistance not only are the minimal infectious or colonization doses of pathogenic or resistant bacteria considerably lower, but animals also excrete these bacteria in higher numbers and over a longer period of time compared to animals with an intact colonization resistance (van den Bogaard and Stoppinger, 1999).

Some data had been reported on antimicrobial susceptibility and emergence of resistant bacteria with low doses of antimicrobials (Rollins et al., 1975; Mamber and Katz, 1985; Corpet, 1987; Tancrede and Barakat, 1989).

Tetracyclines, in relatively low doses, had some impact on the fecal anaerobic micro-biota of humans (WHO, 1991; Waltner-Toews and McEwen, 1994). A close relationship between tetracycline, streptomycin, gentamicin and chloramphenicol residues and the resistance of bacteria isolated from the samples was found, suggesting that the presence of low levels of antimicrobials might exert a positive pressure towards the selection and expression of resistance in bacteria colonizing animal tissues (Vazquez-Moreno et a l 1990). It is possible, although not proven, that low doses of antimicrobial drugs could alter intestinal enzyme activity and had an effect on certain hormones and drugs (Gorbach, 1993).

#### 4.5.2. Hypersensitivity reactions

Drug hypersensitivity was defined as an immune-mediated response to a drug agent in a sensitized patient, and drug allergy is restricted to a reaction mediated by IgE (Riedl and Casillas, 2003). Drugs are foreign molecules, but their molecular weight is usually too small to be immunogenic. For drugs to be immunogenic, they must act as haptens, which must combine with carrier proteins to be immunogenic and elicit antibody formation (Dewdney etal., 1991). Immunologic reactions may manifest from life-threatening anaphylactic reactions to milder reactions, such as rashes. Drug-induced allergic reactions may occur acutely (within 60 min of challenge), sub acutely (1-24 h), or as latent responses (1 day to several weeks). The acute and some sub acute disorders are often due to Type I (IgE)- mediated reactions and, more rarely, due to IgG antibodies (Type II). Immune complex disorders (Type III) are much rarer in this context. Type IV (cell mediated) responses develop more slowly. The principal types of disorder are: Type I: anaphylactic shock, asthma and angioneurotic edema; type II: hemolytic anemia and

agranulocytosis; type III: serum sickness and allergic vasculitis, and type IV: allergic dermatitis (Dayan, 1993; Riedl and Casillas, 2003). In anaphylaxis exposure rapidly leads to severe acute bronco constriction, often risking a degree of asphyxia, marked hypotension, possibly edema at the site of challenge, and severe general illness (Dayan, 1993). Antimicrobial drug residues in animal tissues may cause hypersensitivity reactions in humans. 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 (Dewdney et al., 1991; Sundlof et al., 2000).

Notwithstanding their non-toxic nature, B-lactams appear to be responsible for most of the reported human allergic reactions to antimicrobials (WHO, 1991; Sundlof, 1994; Fein et al., 1995). Aminoglycosides, sulphonamides and tetracyclines may also cause allergic reactions (Paige et al., 1997). Certain macrolides may in exceptional cases be responsible for liver injuries, caused by a specific allergic response to macrolide metabolite-modified hepatic cells (Dewdney et al., 1991).

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 (Tscheuschner, 1972; Kanny et al., 1994; Raison-Peyron et al., 2001). In one case anaphylaxis was possibly caused by streptomycin residues (Tinkelman and Bock, 1984), and angioneurotic edema and tightness of chest by penicillin residues in meat (Schwartz and Sher, 1984). Failure to associate minor reactions, e.g. urticaria, with exposure to allergenic residues may be one reason for the lack of reported cases, although it might also be due to a genuine dearth of reactions (Woodward, 1991). Harmful effects of chloramphenicol observed in association with clinical use in humans include dose-related, reversible suppression of the bone marrow, gray baby syndrome, which is a circulatory collapse in children less than 30 days on high doses, and irreversible, idiosyncratic, non-dose related aplastic anemia (Schmid, 1983; WHO, 1988; Waltner-Toews and McEwen, 1994). Aplastic anemia could occur in susceptible individuals exposed to concentrations of chloramphenicol that might remain as residues in edible tissues of chloramphenicol-treated animals (Settepani, 1984). Aminoglycosides can produce damage in urinary, vestibular and auditory functions (Clark, 1977; Shaikh and Allen, 1985). Toxic and

allergic reactions in humans and animals caused by tetracyclines have only been observed at therapeutic doses (Berends et al., 2001).

#### 4.6. Public health importance of antimicrobial residues in livestock and poultry

Administration of drugs to food-producing animals requires not only consideration of effects on livestock and poultry but also effects on humans who consume food from these livestock and poultry. In short, after food-producing animals have been exposed to drugs in order to cure or prevent disease or to promote growth, the effects of the residues of such treatment may have on humans should be known. These residues consist of the parent compound or compounds derived from the parent drug (or both) including metabolites and residues bound to macromolecules (Weber, 1982).

Concern has been expressed about possible harmful effects on humans through the use of Drugs are as follows:

- I. Increased microbial drug resistance,
- II. Drug residues in food,
- III. Allergic reactions and sensitization to antimicrobials, and
- IV. Drug toxicity (Black, 1984).

Antimicrobial residues in foods of animal origin may cause problems for several reasons. In addition to toxicity, effects on intestinal microbiota and the immune system are important (Gorbach, 1993; Waltner-Toews and McEwen, 1994; Perrin-Guyomard et al., 2001).

## 5. Conclusion

In the age of global antibiotic health hazard, securing public health and to generate confidence that we are practicing medicine in their best interests is the prime target area of veterinarians. Both veterinarians and food producers have become extremely conscious for the need of high public confidence in the products they produce. The surveillance study in target areas indicated that a large number of antibiotics were frequently used for treating various infections in both dairy and poultry industry'. In addition, stakeholders involved do not adhere to withdrawal periods. None adhere to withdrawal period is the major cause of chemical residues. These practices provide conditions favorable to the selection and spread of resistant bacteria and resistant genes. Many management strategies can be implemented to reduce the need for antimicrobials in food animals. Evidence suggested that more judicious use of antimicrobials in food producing animals will reduce the selection of resistant bacteria and help to preserve these valuable drugs for both human and veterinary medicine. Addressing this issue of antimicrobialresistance is one of the most urgent public priorities today. National authorities should adopt a proactive approach that promotes programs aimed at reducing the news for antimicrobials in food animals and ensuring their prudent use. Antimicrobial agents are critical resources for controlling a great number of infection diseases in both animals and the continued availability of effective antimicrobials for humans and animals will ultimately depends upon the responsible use of these products. This necessitates that all effort including awareness creation, observance of withdrawal period, effective surveillance, monitoring and control on the use of veterinary drugs to prevent drug residues in animal derived products be employed.

## **<u>6. Recommendations</u>**

Indiscriminate or excessive use of drugs should be restricted through education and motivation of broiler farmers and practicing veterinarians. Veterinarians should be more rigorous when prescribing veterinary medicinal products and aware of the rules for the prudent use of antimicrobials. Owners should respect the prescribed withdrawal periods of drugs. It is also necessary to organize seminars on the risk of the excess use of antimicrobial substances in food animals for public health. Drug withdrawal periods should be strictly maintained before slaughtering the birds for human consumption.

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