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Review Article

Review on the Antimicrobial Resistance and its Effects on Public Health

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Abstract

Any edible part of an animal product that contains the parent chemicals, their metabolites, and related contaminants of veterinary medications is said to have antimicrobial resistance (AMR). If humans consume a concentration level higher than the standard residual limits, there may be serious effects. Foods derived from animals that have received veterinary medicine are said to include residues of veterinary medicines, which are described as pharmacologically active compounds, principles, or breakdown products and their metabolites. Antibiotic overdose, incorrect drug administration routes, and withdrawal period violations are the most frequent reasons why food derived from animals may include antibiotic residues. If antibiotics are used as "insurance" against disease-related livestock losses, antibiotic use and the presence of antibiotic residues in food products can be hard to control. These kinds of situations are common in many poor countries, where the need for antibiotics rises due to the incidence of infectious diseases. Products made from animals that have these residues in them may cause hypersensitivity reactions, bone marrow depression, cancer, mutagenicity, teratogenicity, and disturbance of normal gut flora. They may also cause increased resistance to antibiotic treatments. Strict observance of AMR limits and withdrawal periods is necessary to guarantee that animal products are safe for human consumption. Therefore, to supervise the use of antimicrobial drugs in the fight against illness, a single regulatory framework is required. The prevalence and effects of drug resistance and antibiotic use on public health are discussed in this review article.

Keywords: Antimicrobials, Antibiotic drugs, Antimicrobial resistance

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Introduction

Antibiotics are substances that either stop or eliminate germs from growing naturally, synthetically, or in a similar semi-synthetic manner. Antibiotics have been widely employed in the dairy, cattle, poultry, aquaculture, and honey production industries worldwide due to their accessibility and affordability. Antibiotics are used in veterinary medicine for medicinal, preventative, nutritional, and growth-related purposes. *Salmonella* species and *Campylobacter jejune* are the main zoonotic infections to watch for the emergence of antibiotic resistance (1).

Veterinary drugs are a necessary part of livestock production because they are used in the therapeutic and preventive treatment of diseases, to modify physiological functions (e.g., growth promoters and tranquilizers), to enhance growth and productivity, and to ensure food safety (2). Worldwide usage of veterinary drugs, which include a variety of chemical constituents such as vaccinations, antimicrobials, antiparasitics, and agonists, is common (3). By enabling earlier weaning, higher animal densities, carcass yield, and meat quality, as well as the use of less expensive feed sources, these medications have been employed to boost the profitability and productivity of modern food-animal production (3). According to several studies (4,5), tetracyclines, amprolium, penicillin, streptomycin, sulphonamides, tylosin, aminoglycosides, -lactams, macrolides and lincosamides, quinolones, sulfonamides, and tetracyclines are among the antimicrobials frequently used in livestock production. Antiparasitic medications include anthelmintics, coccidiostats, stilbenes, amphenicols, nitrofurans, nitroimidazoles, carbamates, pyrethroids, and sedatives.

The ability of drugs to fight infectious bacteria that can be transferred to humans by either direct contact with the sick animal, consumption of food tainted with animal pathogens, or proliferation into the environment is related to the benefit to human health of the proper use of antibiotics in food animals. Drug administration to animals is essential to their health and welfare. Antimicrobial usage in food animals, however, is not without dangers. The primary veterinary medications with the potential to contaminate food are antimicrobials, growth promoters, sedatives, anticoccidials, nonsteroidal anti-inflammatory medicines (NSAIDs), and anti-helminthics. Antimicrobial

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resistance (AMR), a growing issue on a global scale, is the capacity of microorganisms to live and procreate in the presence of antibiotic doses that were once believed to be effective against them.

According to Chuanchuen et al (6), AMR, which affects both human and veterinary medicine, has now reached alarming levels in much of the world and is a serious developing danger to food security and public health. Even if the world's livestock production has been expanding quickly and moving more and more toward a situation where the use of antibiotics (AMU) is a necessary component of production, their improper or excessive usage may result in the development of antibiotic-resistant bacteria (7), the most common veterinary medicines that could contaminate food.

According to research conducted over the past 40 years, AMR in East Africa is linked to human-animal contact, high levels of antibiotic use in small production systems, a lack of a withdrawal period before humans can consume meat and dairy products from recently treated animals, and frequent or negligent AMU, which is said to be one of the main causes of the infectious diseases that initially caused AMR's failure to treat. In Ethiopia, drug usage is widespread across many industries, including veterinary and public health, and there is little oversight of medicines by the government or information on actual reasonable drug use concerning veterinary medicine. Furthermore, foodstuffs may include antibiotic-resistant bacteria and serve as excellent vectors for the spread of antibiotic-resistant strains. As a result, food is a vital medium for the highly effective transfer of AMR factors to consumers' digestive tracts (8). The well-documented spread of AMR bacteria to people through the food chain and from livestock suggests that these animals and the products they produce, such as milk and meat, may operate as reservoirs for human illnesses (9).

In the food supply chain, several viruses that are resistant to antibiotics and can infect and spread to humans have recently appeared. One of them, antibiotic resistance in *Escherichia coli*, *Salmonella*, and *Staphylococcus aureus*, is troublesome for the global healthcare system (10). In veterinary and public health settings, other studies done in Ethiopia also found fragmented considerable prevalence and antimicrobial susceptibility of *Salmonella*, *E. coli*, and *S. aureus* (11).

Therefore, the objectives of this review article are as follows:

- Reviewing the occurrence of antimicrobial drug resistance and its impact
- Providing an overview of the public health impacts of antimicrobial and drug resistance

Public Health Impacts

Public Health Impacts

Because treatment fails when resistant germs emerge, consuming such food products carries a significant danger to one's health. Among these are the spread of bacteria resistant to antibiotics, immunopathological consequences, autoimmunity, carcinogenicity (of methazine, oxytetracycline, and furazolidone), mutagenicity, nephropathy (of gentamicin), hepatotoxicity, toxicity to the bone marrow (of chloramphenicol), and allergy (of penicillin).

The Development of Drug Resistance

Antibiotic-containing animal feeds have been shown to cause AMR, which can make medical treatments ineffective for both humans and animals. Drugs have reportedly been known to be utterly ineffective in some circumstances. Given the documented fact that microbial resistance can be transferred from animals to humans (12), resistant microorganisms can enter humans directly through contact or indirectly through animal products and byproducts (e.g., milk, eggs, etc).

Allergy or Hypersensitivity Reactions

A patient who has become sensitized to a chemical substance may develop an allergy or an immune-mediated reaction (such as a medication). These allergic reactions, which are typically mediated by IgE, may occur after medications or macromolecules like protein, fats, and carbs are administered. It has been confirmed that an estimated 4%-11% of people in the world are thought to be penicillin allergic. People in this category who eat animal products that contain residues of penicillin run the risk of becoming allergic, which can cause a skin rash or potentially life-threatening anaphylaxis (12). According to the study of Thong and Tan (13), IgE-mediated allergic anaphylaxis is associated with penicillin and other anesthetic medicines once they are administered during surgical periods. Human exposure to sulfonamide can cause a range of skin reactions, from mild rash to severe taxidermic.

Carcinogenic Effect

Any chemical or agent that can change an organism's genetic composition, causing it to proliferate and become cancerous, is referred to as a carcinogen; on the other hand, a carcinogen is any substance that encourages carcinogenesis, the development of cancer, or has carcinogenic activity. According to the studies of conducted by Aiello et al (14) and Bendesky (15), carcinogenic residues work by covalently attaching intracellular elements such as proteins, glycogen, phospholipids, DNA, and RNA. Diethylstilbestrol (DES), a hormone-like substance used to produce food for animals, was outlawed due to its potent carcinogenic properties. The International Agency for Research on Cancer (IARC) states that there is ample evidence to imply that metronidazole causes cancer in animals, but

not enough to support this claim in people (16).

Disruptions of Normal Intestinal Flora

Intestinal micro flora plays an important role in human physiology. They establish control and prevent the colonization of pathogenic bacteria in the gastrointestinal tract. However, studies have shown that antimicrobials administered for therapeutic purposes can potentially alter or change the ecological composition of the intestinal flora. 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 humans in the diagnosis of gastrointestinal disorders (17,18).

Mutagenic Effect

Mutagens are chemicals or substances with the potential to cause mutations in a DNA molecule, thereby altering the genetic makeup of a cell or organism. Studies have shown that alkalizing agents and analogous DNA bases are mutagenic. There is a growing fear of a possible drug-related gene mutagen or chromosome breakage among the human population (19-21).

Teratogenic Effect

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

Impact on the Global Economy

Antimicrobials' usage in livestock, either at sub-therapeutic or therapeutic dosages, and their 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 the body's functional and system integrity (i.e., endocrine, nervous, reproductive, and immune systems) (22,23), resulting from the consumption of such 'compromised' food of animal origin, has reduced consumers' confidence and resulted in adverse impacts on the global economy.

Impact of Antibiotic Resistance and Ways of Prevention

The fight against antibiotic resistance has been acknowledged as a top concern for public health worldwide. The World Health Organization (WHO) published a global action plan on antibiotic resistance in 2016 and advised every nation to create its own. We need to take the issue of antibiotic resistance very seriously if we hope to keep antibiotics as an important therapeutic tool. Treatment of resistant infections is linked to longer hospital stays, more expensive second-line medication, and more research. Productivity losses as a result of extra morbidity and mortality are additional indirect costs linked to AMR (24,25). There is a tested and effective approach to the problem of antibiotic resistance: simply phase out the use of antibiotics as routine animal feed additives and limit the damage that arises from antibiotic use. We know that agricultural antibiotic use increases the human carriage of resistant organisms and that phasing out this use results in a markedly decreased incidence of human carriage (26).

Some studies have shown that agricultural antibiotic use may be more important than hospital antibiotic use in generating the asymptomatic carrier state. The discovery of new antimicrobials as well as strategies to expand the useful life of existing antibiotics is important to combat the ever-increasing AMR (27-29).

Antimicrobials pass into every tissue and fluid of the body before being excreted. High levels of antibiotic residues were detected in milk and meat destined for human consumption. In Ethiopia, 70.58% of farms in Debre Zeit and 83.33% of farms in Nazareth have the Oxytetracycline level; similarly, in 20.58% of the farms found in Debre Zeit and 16.16% of the farms found in Nazareth, the penicillin G level was above the maximum residue limit established by FAO. In another study conducted on poultry meat, 27.4% of chickens contained Oxytetracycline. Other studies were also conducted in Ethiopia, in which Oxytetracycline and penicillin G were obtained from milk and tetracycline was obtained from beef (30,31). Application of veterinary drugs in livestock production is inevitable as they are essential for the treatment and prevention of diseases, modification of physiological functions, improvement of growth and productivity, as well as ensuring food safety (32,33).

Conclusion and Implications

Veterinary antibiotics are commonly used to treat and prevent a wide range of bacterial diseases in both humans and animals. It also exposes slivers of proof regarding the unreasonable use of antibiotics in the dairy industry and the consumption patterns of raw milk. The primary causes of the high prevalence of resistant strains are human management practices, including inappropriate use, such as the use of antibiotics at sub-therapeutic levels or for short periods, failure to adhere to the withdrawal period and overdose, and extra-label or illegal drug applications. Ultimately, it is thought that the establishment of ongoing resistance surveillance programs throughout the nation is required, given the significant levels of resistance now identified.

Since antimicrobial medications are used to treat and prevent animal diseases outside of farms, the existence of veterinary antibiotic resistance in food items is a global

health problem. Antibiotic residues in foods including milk, eggs, and meat can generally lead to antibiotic usage in animals. These residues have the potential to cause several adverse effects, including immunopathological effects, nephropathy (gentamicin), hepatotoxicity, reproductive disorders, toxicity to the bone marrow (chloramphenicol), carcinogenicity (sulfamethazine, oxytetracycline, and furazolidone), and even mutagenicity. Therefore, coordinated regulatory organizations are needed to monitor the use of antimicrobial medications to control infections and implement penalties for indiscriminate consumption to address the issue of AMR.

Based on the above remarks, the following implications need to be considered:

- To ensure the quality of raw milk, meat, and eggs, everyone engaged in the milk and dairy production chain should be trained in hygienic practices.
- Indiscriminate and irrational use of antibiotics in beef cattle without following a withdrawal period may result in unexpected resistance in beef meat and cause serious health hazards to consumers.
- All efforts, including the education of beef farm owners about the proper utilization of antimicrobials, the side effects of the irrational use of drugs, the observance of the withdrawal period, effective surveillance, monitoring, and control of the use of veterinary drugs to prevent drug resistance in beef meat, are recommended.
- To protect consumers from AMR, food safety management programs should be implemented and highly considered.
- Cooking and freezing procedures are important in the inactivation of antibiotic resistance because the heat treatment of animal foodstuffs may inactivate antibiotics.
- Public awareness should be given on the proper use, handling, and storage of antibiotics, which should be prioritized for livestock farmers and other drug users.
- Every country should adopt laws on antibiotic usage in animals and their resistance limits in foods.

Authors' Contribution

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Competing Interests

In this study, there is no conflict of interest in publishing this manuscript.

Ethical Approval

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References

1. Smith GW, Gehring R, Riviere JE, Yeatts JL, Baynes RE. Elimination kinetics of ceftiofur hydrochloride after intramammary administration in lactating dairy cows. J Am Vet Med Assoc. 2004;224(11):1827-30. doi: 10.2460/javma.2004.224.1827.
2. World Health Organization (WHO). WHO Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals. Geneva: WHO; 2017.
3. Moreno L, Lanusse C. Veterinary drug residues in meat-related edible tissues. In: Purslow PP, ed. New Aspects of Meat Quality. Woodhead Publishing; 2017. p. 581-603. doi: 10.1016/b978-0-08-100593-4.00024-2.
4. Landoni MF, Albarellos G. The use of antimicrobial agents in broiler chickens. Vet J. 2015;205(1):21-7. doi: 10.1016/j.tvjl.2015.04.016.
5. Alhaji NB, Haruna AE, Muhammad B, Lawan MK, Isola TO. Antimicrobials usage assessments in commercial poultry and local birds in north-central Nigeria: associated pathways and factors for resistance emergence and spread. Prev Vet Med. 2018;154:139-47. doi: 10.1016/j.prevetmed.2018.04.001.
6. Chuanchuen R, Pariyotorn N, Siriwattanachai K, Pagdepanichkit S, Srianga S, Wannaprasat W, et al. Review of the Literature on Antimicrobial Resistance in Zoonotic Bacteria from Livestock in East, South and Southeast Asia. Bangkok. FAO Regional Office for Asia and the Pacific; 2014.
7. Phu VD, Wertheim HF, Larsson M, Nadjm B, Dinh QD, Nilsson LE, et al. Burden of hospital acquired infections and antimicrobial use in Vietnamese adult intensive care units. PLoS One. 2016;11(1):e0147544. doi: 10.1371/journal.pone.0147544.
8. Spanu V, Spanu C, Virdis S, Cossu F, Scarano C, De Santis EP. Virulence factors and genetic variability of *Staphylococcus aureus* strains isolated from raw sheep's milk cheese. Int J Food Microbiol. 2012;153(1-2):53-7. doi: 10.1016/j.ijfoodmicro.2011.10.015.
9. Normanno G, La Salandra G, Dambrosio A, Quaglia NC, Corrente M, Parisi A, et al. Occurrence, characterization and antimicrobial resistance of enterotoxigenic *Staphylococcus aureus* isolated from meat and dairy products. Int J Food Microbiol. 2007;115(3):290-6. doi: 10.1016/j.ijfoodmicro.2006.10.049.
10. Kashef N, Esmaeeli Djavid G, Shahbazi S. Antimicrobial susceptibility patterns of community-acquired uropathogens in Tehran, Iran. J Infect Dev Ctries. 2010;4(4):202-6. doi: 10.3855/jidc.540.
11. Hailu D, Gelaw A, Molla W, Garedew L, Cole L, Johnson R. Prevalence and antibiotic resistance patterns of *Salmonella* isolates from lactating cows and in-contact humans in dairy farms, Northwest Ethiopia. J Environ Occup Sci. 2015;4(4):171-8. doi: 10.5455/jeos.20151102014711.
12. Baynes RE, Dedonder K, Kissell L, Mzyk D, Marmulak T, Smith G, et al. Health concerns and management of select veterinary drug residues. Food Chem Toxicol. 2016;88:112-22. doi: 10.1016/j.fct.2015.12.020.
13. Thong BY, Tan TC. Epidemiology and risk factors for drug

allergy. Br J Clin Pharmacol. 2011;71(5):684-700. doi: 10.1111/j.1365-2125.2010.03774.x.
14. Aiello SE, Lines PR, Kehn CM. Anthelmintics. In: The Merck Veterinary Manual. 9th ed. Kenilworth, NJ: Merck & Co Inc; 2005. p. 2111-24.
15. Bendesky A, Menéndez D, Ostrosky-Wegman P. Is metronidazole carcinogenic? Mutat Res. 2002;511(2):133-44. doi: 10.1016/s1383-5742(02)00007-8.
16. Cotter PD, Stanton C, Ross RP, Hill C. The impact of antibiotics on the gut microbiota as revealed by high throughput DNA sequencing. Discov Med. 2012;13(70):193-9.
17. Foster W, Beecroft ML. Chemical Exposures and Human Fertility. Infertility Awareness Association of Canada; 2014.
18. Horrigan L, Lawrence RS, Walker P. How sustainable agriculture can address the environmental and human health harms of industrial agriculture. Environ Health Perspect. 2002;110(5):445-56. doi: 10.1289/ehp.02110445.
19. Kaier K, Frank U. Measuring the externality of antibacterial use from promoting antimicrobial resistance. Pharmacoeconomics. 2010;28(12):1123-8. doi: 10.2165/11535640-000000000-00000.
20. Aarestrup FM, Seyfarth AM, Emborg HD, Pedersen K, Hendriksen RS, Bager F. Effect of abolishment of the use of antimicrobial agents for growth promotion on occurrence of antimicrobial resistance in fecal enterococci from food animals in Denmark. Antimicrob Agents Chemother. 2001;45(7):2054-9. doi: 10.1128/aac.45.7.2054-2059.2001.
21. Smith DL, Dushoff J, Morris JG Jr. Agricultural antibodies and human health: does antibiotic use in agriculture have a greater impact than hospital use? Int J Risk Saf Med. 2005;17(3-4):147-55.
22. Bedada AH, Zewde BM, Zewde BM. Tetracycline residue levels in slaughtered beef cattle from three slaughterhouses in central Ethiopia. Glob Vet. 2012;8(6):546-54.
23. Agmas B, Adugna M. Antimicrobial residue occurrence and its public health risk of beef meat in Debre Tabor and Bahir Dar, Northwest Ethiopia. Vet World. 2018;11(7):902-8. doi: 10.14202/vetworld.2018.902-908.
24. Garedaghi Y, Firouzivand Y, Hassanzadeh Khanmiri H, Shabestari Asl A. A review of the most important antiparasitic compounds effective on human fascioliasis from the past until now. Curr Drug Ther. 2023;18(5):365-76. doi: 10.2174/1574885518666230403111528.
25. Garedaghi Y, Khaki A, Feizi A, Abbas Raza SH, Khan R, Hao L, et al. Epidemiological and pathological studies on the helminthic parasites in native chickens of Tabriz city, Iran. Genet Mol Res. 2017;16(4):gmr16039824. doi: 10.4238/gmr16039824.
26. Garedaghi Y, Firouzivand Y, Heikalabadi M. Assessment of *Neospora caninum* seroprevalence in buffalo in Tabriz city, north-west of Iran. Buffalo Bull. 2017;36(2):379-84.
27. Garedaghi Y, Firouzivand Y, Luca I. Prevalence of endoparasites and their zoonotic significance in wild rabbits of Ahar city, Iran. Am J Anim Vet Sci. 2022;17(1):31-4.
28. Garedaghi Y, Shojaee S, Khaki A, Hatef A, Ahmadi Ashtiani HR, Rastegar H, et al. Modulating effect of *Allium cepa* on kidney apoptosis caused by *Toxoplasma gondii*. Adv Pharm Bull. 2012;2(1):1-6. doi: 10.5681/apb.2012.001.
29. Garedaghi Y, Bahavarnia SR. Repairing effect of *Allium cepa* on testis degeneration caused by *Toxoplasma gondii* in the rat. Int J Womens Health Reprod Sci. 2014:2(2):80-9. doi: 10.15296/ijwhr.2014.12.
30. Garedaghi Y, Firouzivand Y. Assessment of pregnant women toxoplasmosis by ELISA method in Miandoab city, Iran. Int J Womens Health Reprod Sci. 2017;5(1):72-5. doi: 10.15296/ijwhr.2017.13.
31. Garedaghi Y, Khayatnouri M, Safarmashaei S. The effect of ivermectin pour-on administration against natural *Dictyocoulus viviparous* infestations and prevalence rate of that in cattle. Adv Environ Biol. 2011:5(7):1821-5.
32. Garedaghi Y, Rezaii Saber AP, Saberie Khosroshahi M. Prevalence of bovine cysticercosis of slaughtered cattle in Meshkinshahr Abattoir, Iran. J Anim Vet Adv. 2012;11(6):785-8.
33. Santiago-Figueroa I, Lara-Bueno A, González-Garduño R, de Gives PM, Delgado-Núñez EJ, de Jesús Maldonado-Simán E, et al. Anthelmintic evaluation of four fodder tree extracts against the nematode *Haemonchus contortus* under in vitro conditions. Rev Mex Cienc Pecu. 2023;14(4):855-73.