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Antibiotics Used in Food Animals: A review

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ABSTRACT: Veterinary medications, particularly antibiotics, are crucial elements in the manufacturing of animal feed. Typically, antibiotics are mostly employed in animals for the purpose of treating and preventing infections, as well as promoting growth. The utilization of antibiotics in animals can lead to the presence of antibiotic residues in food products, including milk, eggs, and meat. It is possible for these residues to cause a lot of bad things, like the spread of bacteria that are resistant to antibiotics to humans, immune system problems, allergies, and even cancer (with sulphamethazine, and other drugs). The most harmful consequence of residual drugs is the transfer of resistant antibiotic germs to individuals, aided by the mobility traits of resistance. Controlling the consumption of antibiotics in cattle is imperative in order to mitigate these detrimental effects. The issue should be communicated to individuals and local protocols through formal education. This review will discuss the use of antibiotics in food products and their effects on the health of people.

Keywords: Antibiotics, Veterinary drugs, Antibiotic Residues, Food

1. INTRODUCTION

Veterinary drugs, particularly antibiotics, are crucial molecules in the context of production to animal feed [1]. Around 80 % of animals employed in the process of producing food are now administered veterinary medications at some point or throughout their lifespan [2].

Antibiotics are pharmacological compounds that effectively treat bacterial infections in both people and animals [3]. They operate by either eliminating the bacteria or inhibiting its capacity to propagate and multiply [4]. Antibiotics, in particular, are among the most essential components in the manufacture of animal feed. Antibiotics are typically used mostly in animals to treat and prevent infections as well as to promote growth. Meat, eggs, and milk products may include antibiotic residues from animal use of antibiotics [5].

These residues can cause various negative effects, such as immunopathological impacts, allergies, mutagenicity, nephropathy (in the case of gentamicin), hepatotoxicity, problems with reproduction, bone marrow toxic effects (in the case of chloramphenicol), as well as carcinogenicity (in the case of sulfamethazine, and other drugs) [6-8]. Antibiotics can be administered through various methods:

1. Administered by the oral route. The available options include tablets, capsules, or liquid formulations [9].
2. In terms of subject matter. This product may come in the form of a cream, spray, or ointment that is topically applied to the skin. Alternatively, it may also refer to ocular ointment, ocular drops, or auricular drops [10].
3. Administered via injection or intravenous (IV) route. Typically, this is reserved for more severe infections [11].

2. Major classes of antibiotics

These sometimes-complicated molecules could have several functions within each one. Antibiotics can therefore be neutral, cationic, anionic, or zwitterionic, depending on the pH. Antibiotics can be classified based on their mode of action or chemical composition. They are separated into several subgroups, including [12, 13]:-

Aminoglycosides: act by binding to the aminoacyl site of 16S ribosomal RNA within the 30S ribosomal subunit, leading to misreading of the genetic code and inhibition of translocation.

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Tetracyclines: inhibit the 30S ribosomal subunit, hindering the binding of the aminoacyl-tRNA to the acceptor site on the mRNA-ribosome complex.

Macrolides: are protein synthesis inhibitors. The mechanism of action of macrolides is inhibition of bacterial protein biosynthesis, and they are thought to do this by preventing peptidyltransferase from adding the growing peptide attached to tRNA to the next amino acid.

Mphenicols: Inhibition of protein synthesis. Chloramphenicol irreversibly binds to a receptor site on the 50S subunit of the bacterial ribosome, inhibiting peptidyl transferase.

β-lactams: Inhibition of cell wall synthesis. This particular group is characterized by its four-membered, nitrogen-containing ß-lactam ring at the core of their structure, which is key to the mode of action of this group of antibiotics.

Fluoroquinolones: Inhibition of nucleic acid synthesis. Fluoroquinolones have been shown to bind to the DNA gryrase-DNA complex and interrupt a process that leads to the negative supercoiling of bacterial DNA.

Glycopeptides: Inhibition of cell wall synthesis. Glycopeptides bind to precursors of cell wall synthesis which leads to interference of the penicillin-binding protein (PBP) enzymes such as transpeptidases to incorporate the precursors into the growing cell wall.

3. Utilization of Antibiotics in Food Products

Antibiotics are employed in the realm of food production, particularly in animals, to yield several advantages, such as enhancing animal welfare, improving carcass quality, optimizing growth efficiency, promoting economic productivity, and safeguarding public health [14, 15]. Antibiotics are effective in preventing and/or treating infectious illnesses in animals. These medications can enhance animal performance by decreasing the physiological expenses associated with development limitations caused by both mild and severe diseases. Antibiotic treatment effectively controls significant infections, including E coli, Enterococcus and other types [16]. The primary advantage to human health is the prevention of serious diseases that are able to be transmitted to persons by interacting with sick animals, consumption of food that has been tainted, or environmental spread [17].

4. Identification of Antimicrobial Waste products in Food

Two distinct approaches for determining antibiotic antimicrobial waste products [18]:

(I) confirmation; (ii) screening techniques.

Confirmatory techniques rely on the combination of (LC) and (MS). Utilizing ultraviolet (UV) detection, liquid chromatography (LC) can be beneficial for analyzing drug residues in food. Several investigations have demonstrated the efficacy of capillary electrophoresis (CE) in detecting antibiotic residues [19].

Screening methods can be categorized into two types: microbiological assays and immunoassays. Quantitative or partially quantitative microbial assays depend on a specific interaction between a susceptible organism and the antibiotic [20, 21]. These methods provide unique advantages, such as dependability, cost-effectiveness, and simplicity. Unlike LC-MS, these tests possess the capacity to identify any antibiotic or its active metabolite, whereas LC-MS is commonly employed to study compounds that have been deliberately selected as targets [22]. These procedures have several benefits. They allow non-professionals to conduct microbiological testing, and only a few tests necessitate sample treatment. Additionally, these tests can be conducted using either a tube or a microplate.

5. kind of immunity exist in animals

Each animal have a rudimentary immune system that defends against specific pathogens to which they are susceptible. Innate immunity, or natural immunity, is a dual defense mechanism. The humoral innate immunity is mediated by a collection of molecules present in the humors, which are the body fluids [23].

6. Role of animals: passive immunity

Passive immunity refers to the passage of preexisting antibodies from one specific animal to another, such as from an animal that is the host to a recipient animal, which may be an offspring or another species altogether [24].

7. Antibiotic usage in animals

Animals utilize antibiotics primarily for three purposes: as growth promoters for improving feed utilization and production; as therapeutics to treat sick animals; and as prophylactics to prevent animal infections [25]. Therapeutic therapy generally entails administering antibiotic doses to individual animals for short periods of time that surpass the minimal inhibitory concentration of the pathogen, whether it is known or suspected [26]. Therapeutic treatment is often given to animals raised in critical care through food or drink; however, in certain cases, the effectiveness of this approach may be questioned because unwell animals frequently refuse food or drink. Once more, prophylactic treatment is administering moderate to high dosages of antibiotics to a group of animals via feed or water for a certain amount of time. Antibiotics used as growth promoters are typically purchased over-the-counter by feedmakers and farmers [27].

8. Antibiotic Residues in Foods

Antibiotic residues have been detected in animal tissues such as blood when high quantities of the drugs were utilized. But since the antibiotics can be quickly removed—they vanish from the animals' blood and tissue in a matter of daysafter they are fed a nonmedicated diet [28].

When preparing, storing, and transporting feed made from animal sources, direct contamination from the air and water is possible. One example of indirect contamination is the presence of antibiotics in animal feed.

During the farming operation, rainwater or the waste treatment system may introduce resistant microbes into rivers and other water sources. Antibiotics are, in fact, excreted in both human and animal urine. Antibiotics may therefore also find their way into waterways through agricultural waste, which could lead to additional selection of species that are resistant.Antibiotic use is widespread in fish farming, and fish used for food may be tainted with resistant microbes [6].

Cooking has a crucial role in diminishing the quantity of antibiotic residues in food, as most animal-derived foods are not consumed in their raw state.

9. Adverse Impact of Antibiotic Waste products in Food

Allergic responses are a significant and crucial negative consequence of antibiotics in food. A significant number of medicines and antibiotics have the potential to trigger allergic responses [29]. Most of the information pertains to the hypersensitivity of penicillin, aminoglycosides, and tetracyclines. Regrettably, the enduring consequences of antibiotics on human health remain unknown.

Sensitivity responses are among the most effects of significant negative of antibiotics in food. Allergic reactions are possible with several medications and medicines. Most of the information relates to tetracycline, aminoglycoside, and penicillin hypersensitivity [6].

Antibiotics beta-lactams are regarded as less amount of hazardous. However, it is determined that they were to blame for the majority of documented allergic reactions in humans resulting from antimicrobials. Harmful Impact of Antibiotic Residues in Food [30]. β-lactams are recognized as antibiotics with lower toxicity. Nevertheless, it has been determined that they are primarily accountable for the majority of documented allergic reactions caused by antimicrobials in humans. Idiosyncratic reactions such as allergies, skin rashes, and phototoxic dermatitis have been observed in relation to the administration of tetracyclines.

10. Antibiotic Resistance Mechanisms

Multiple processes can lead to the development of antibiotic resistance, including mutations in the bacterial cell's current genome, modifications in the proteome, and the production of bacterial cells that interact with plasmids via horizontal gene transfer. Circular DNA molecules known as plasmids have the ability to facilitate horizontal gene transfer across bacteria through conjugation and independent chromosomal replication. Plasmids with additional antibiotic-resistant genes have varying rates of replication based on the type of bacterial host. Horizontal transfer of genes is a method where genetic material is transferred laterally across organisms by direct DNA exchange, serving as an alternative to the horizontal transfer of DNA from parent to child. This stage is vital in the process of bacteria adapting to various environments [31].

11. Prevalence of antibiotic-resistant microorganisms in food and food producing animals and its correlation with the usage of growth promoters

A study of epidemiology that looked at groups of pigs and chickens that were exposed and those that were not found a link between using avoparcin to help animals grow and the number of cases of GRE in food animals. This investigation demonstrated a significant statistical correlation between the discovery of GRE in animals grown on the same farm and the past usage of avoparcin as a growth promoter. It also eliminated a number of additional possible contributing variables. Consequently, a correlation was shown between the usage of an AGP and the prevalence of AGP-resistant bacteria in food animals [32].

Several continents and countries have done follow-up studies on enterococci that were found in animal feces and food that came from animals. These studies have shown that using antibiotics to help plants grow is closely linked to high levels of resistance to antibiotics that are used in medicine, mostly in enterococci. The avoparcin-GRE connection has been the subject of the most studies, but AGPs from other groups of antimicrobials, including macrolides (tylosin and spiramycin), evernimicins (avilamycin), streptogramins (virginiamycin), and bacitracin, have also demonstrated this association [33].

12. Antibiotics serve as stimulants of growth

Numerous theories have been put forth to explain how subtherapeutic antibiotic dosages boost livestock growth. According to Gaskins, giving animals antibiotics at subtherapeutic concentrations helps them use less energy to keep their commensal bacteria in their gastrointestinal tracts, which frees up more energy for growth. The results showing that antibiotic-fed, germ-free, isolated chicks did not grow more quickly lend credence to this assertion. Under typical conditions, intestinal bacteria live in a host's digestive system and have an impact on critical immunological, physiological, and nutritional aspects that preserve the host's general health. Compared to germ-free animals, these gut microorganisms enable animals to have greater defenses against the colonization of harmful bacteria, as well as larger guts, thicker gut walls, and more intestinal villi. Regretfully, the bacteria also raise the turnover of the gut epithelium, decrease the digestion of fat, absorb nutrients, and excrete metabolites. This may result in an overpopulation of bacteria in the small intestine, which can stunt the animals' growth and be linked to malabsorption, weight loss, and poor health [34].

Antibiotics were thought to prevent harmful bacterial development during the animal's growth phase, even at subtherapeutic levels, which enhanced the animal's general health and weight gain. By changing the way the cholyltaurine hydrolase enzyme in the stomach works, antibiotics may work by stopping the growth of metabolites, such as breakdown products of bile. This causes the animals to gain more weight. Antibiotics reduce intestinal wall inflammation and enhance nutrition absorption to enhance the function of the gut barrier. The well-established idea that antibiotics have an anti-inflammatory effect on inflammatory cells lends support to this theory. Determining the precise mode of action of antibiotic growth promoters is still a challenging task. We can conclude that the mechanism of action of antibiotic growth promoters in livestock is through altering the physiological processes and makeup of the gut microbiota [6].

13. Veterinary antibiotics

Strict limits for antibiotic consumption in agriculture are necessary due to the rising incidence of resistant bacteria in the environment and the widespread use of drugs in livestock breeding.

Antibiotics can enter the environment through a variety of sources, including factory emissions, the disposal of unused medication and containers, effluents from pharmaceutical manufacturing, animal waste and animal husbandry, excretory products from pasture-reared animals, aquaculture, and sewage treatment plants [35]. The main entry points for antibiotics into our environment are depicted in Figure 2.

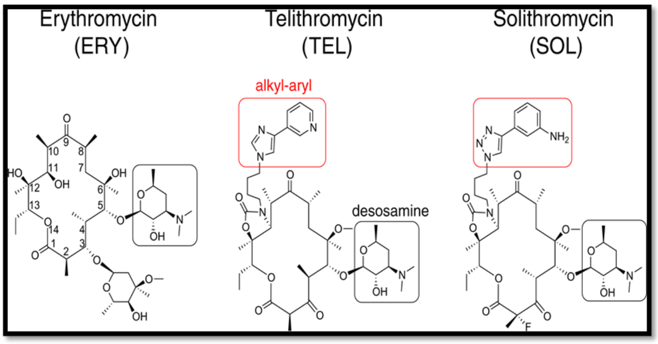

FIGURE 1. - General structure of antibiotics

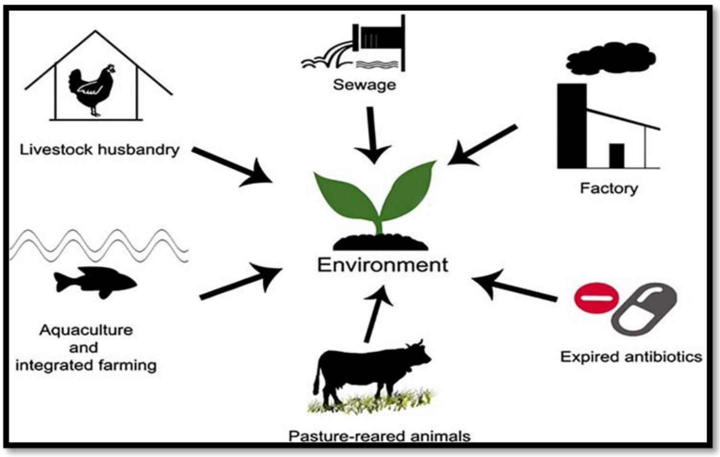

FIGURE 2. - General antibiotic applications fielda

14. Conclusion

The presence of antibiotics in many food products, particularly meat and milk, is a significant concern for human health due to contamination. The utilization of antibiotics in food products continues to increase. It is important to acknowledge that antibiotics included in food may possess inherent toxicity and might have a cumulative impact. Nevertheless, abstaining from the use of antibiotics in animal production carries some hazards. Prior to administration, it is necessary to evaluate the risk-benefit ratio of employing the medicine in living creatures. Implementing a ban on the use of antibiotics in food production may not be a feasible strategy. It is crucial to ensure that relevant authorities regulate the use of antimicrobial agents in animal production. Additionally, before selling and consuming meat and internal organs, it is necessary to examine them for medication residues.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

REFERENCES

[1] M. Bacanlı and N. Başaran, "Importance of antibiotic residues in animal food," Food and Chemical Toxicology, vol. 125, pp. 462-466, 2019. doi.org/10.1016/j.fct.2019.01.033

[2] Z. Lin, R. Gehring, J. Mochel, T. Lave, and J. Riviere, "Mathematical modeling and simulation in animal health–Part II: Principles, methods, applications, and value of physiologically based pharmacokinetic modeling in veterinary medicine and food safety assessment," Journal of veterinary pharmacology and therapeutics, vol. 39, no. 5, pp. 421-438, 2016. doi.org/10.1111/jvp.12311

[3] E. Etebu and I. Arikekpar, "Antibiotics: Classification and mechanisms of action with emphasis on molecular perspectives," Int. J. Appl. Microbiol. Biotechnol. Res, vol. 4, no. 2016, pp. 90-101, 2016. doi: 10.4103/phrev.phrev_21_17

[4] M. J. Cheesman, A. Ilanko, B. Blonk, and I. E. Cock, "Developing new antimicrobial therapies: are synergistic combinations of plant extracts/compounds with conventional antibiotics the solution?," Pharmacognosy reviews, vol. 11, no. 22, p. 57, 2017.

[5] A. Miró-Canturri, R. Ayerbe-Algaba, and Y. Smani, "Drug repurposing for the treatment of bacterial and fungal infections," Frontiers in microbiology, vol. 10, p. 41, 2019. doi.org/10.3389/fmicb.2019.00041

[6] R. Kyuchukova, "Antibiotic residues and human health hazard-review," Bulgarian Journal of Agricultural Science, vol. 26, no. 3, 2020.

[7] T. Tadesse and T. Tadesse, "Public health impacts of antibiotic residues in foods of animal origin: A review," Public Health, vol. 7, no. 10, pp. 6-11, 2017.

[8] S. Jeena, N. Venkateswaramurthy, and R. Sambathkumar, "Antibiotic residues in milk products: impacts on human health," Research Journal of Pharmacology and Pharmacodynamics, vol. 12, no. 1, pp. 15-20, 2020.

[9] D. A. van Riet-Nales, J. A. Ferreira, A. F. Schobben, B. J. de Neef, T. C. Egberts, and C. M. Rademaker, "Methods of administering oral formulations and child acceptability," International journal of pharmaceutics, vol. 491, no. 1-2, pp. 261-267, 2015. doi.org/10.1016/j.ijpharm.2015.06.047

[10] A. P. Raphael, G. Garrastazu, F. Sonvico, and T. W. Prow, "Formulation design for topical drug and nanoparticle treatment of skin disease," Therapeutic Delivery, vol. 6, no. 2, pp. 197-216, 2015. doi.org/10.4155/tde.14.106

[11] L. R. Marks, N. S. Nolan, S. Y. Liang, M. J. Durkin, and M. B. Weimer, "Infectious complications of injection drug use," Medical Clinics, vol. 106, no. 1, pp. 187-200, 2022.

[12] R. Aminov, "History of antimicrobial drug discovery: Major classes and health impact," Biochemical pharmacology, vol. 133, pp. 4-19, 2017.

[13] A. C. Reis, B. A. Kolvenbach, O. C. Nunes, and P. F. Corvini, "Biodegradation of antibiotics: the new resistance determinants–part II," New biotechnology, vol. 54, pp. 13-27, 2020. doi.org/10.1016/j.nbt.2019.08.003

[14] C. G. Scanes, "Animal agriculture: Livestock, poultry, and fish aquaculture," in Animals and human society: Elsevier, 2018, pp. 133-179.

[15] E. N. Ponnampalam and B. W. Holman, "Sustainability II: Sustainable animal production and meat processing," in Lawrie's Meat Science: Elsevier, 2023, pp. 727-798. doi.org/10.1016/B978-0-323-85408-5.00001-7

[16] P. J. Collignon and S. A. McEwen, "One health—its importance in helping to better control antimicrobial resistance," Tropical medicine and infectious disease, vol. 4, no. 1, p. 22, 2019. doi.org/10.7632/tropicalmed9763823.

[17] A. L. Fymat, "Antibiotics and antibiotic resistance," Biomed J Sci & Tech Res, vol. 1, no. 1, pp. 1-16, 2017. doi.org/10.3390/tropicalmed4010022

[18] M. Balouiri, M. Sadiki, and S. K. Ibnsouda, "Methods for in vitro evaluating antimicrobial activity: A review," Journal of pharmaceutical analysis, vol. 6, no. 2, pp. 71-79, 2016. doi.org/10.1016/j.jpha.2015.11.005

[19] B. G. Keevil, "LC–MS/MS analysis of steroids in the clinical laboratory," Clinical biochemistry, vol. 49, no. 13-14, pp. 989-997, 2016.

[20] S. Ahmed et al., "Receptor-based screening assays for the detection of antibiotics residues–a review," Talanta, vol. 166, pp. 176-186, 2017. doi.org/13.2422/ Talanta 867398

[21] R. Parthasarathy, C. E. Monette, S. Bracero, and M. S. Saha, "Methods for field measurement of antibiotic concentrations: Limitations and outlook," FEMS microbiology ecology, vol. 94, no. 8, p. fiy105, 2018.

[22] R. Pratiwi, S. P. Ramadhanti, A. Amatulloh, S. Megantara, and L. Subra, "Recent Advances in the Determination of Veterinary Drug Residues in Food," Foods, vol. 12, no. 18, p. 3422, 2023. doi.org/10.3390/foods12183422

[23] P. Fathima Shameela, "Evaluation of Immunomodulatory Activity of Ethanolic Extract of Annona Recticulata Fruits," Annai JKK Sampoorani Ammal College of Pharmacy, Komarapalayam, 2016.

[24] M. Florin-Christensen et al., "Pursuing effective vaccines against cattle diseases caused by apicomplexan protozoa," CABI Reviews, no. 2021, 2021.

[25] M. Saad and M. B. M. Ahmed, "Necessary usage of antibiotics in animals," Antibiotic Use in Animals, IntechOpen, Janeza Trdine, vol. 9, no. 51000, pp. 9-23, 2018. doi.org/10.1079/PAVSNNR20211602

[26] S. D. Stewart and S. Allen, "Antibiotic use in critical illness," Journal of Veterinary Emergency and Critical Care, vol. 29, no. 3, pp. 227-238, 2019.

[27] S. Nayiga, "Antibiotics in Society: a multi-sited ethnography in rural and urban Uganda," London School of Hygiene & Tropical Medicine, 2022. doi.org/10.17037/PUBS.04664936

[28] M. Girmatsion et al., "Rapid detection of antibiotic residues in animal products using surface-enhanced Raman Spectroscopy: A review," Food Control, vol. 126, p. 108019, 2021.

[29] Q. Zhang, L. Cheng, J. Wang, M. Hao, and H. Che, "Antibiotic-induced gut microbiota dysbiosis damages the intestinal barrier, increasing food allergy in adult mice," Nutrients, vol. 13, no. 10, p. 3315, 2021. doi.org/10.1016/j.foodcont.2021.108019

[30] M. M. J. Arsène et al., "The public health issue of antibiotic residues in food and feed: Causes, consequences, and potential solutions," Veterinary World, vol. 15, no. 3, p. 662, 2022. doi: 10.14202/vetworld.2022.662-671

[31] J. Lu, Y. Wang, M. Jin, Z. Yuan, P. Bond, and J. Guo, "Both silver ions and silver nanoparticles facilitate the horizontal transfer of plasmid-mediated antibiotic resistance genes," Water research, vol. 169, p. 115229, 2020. doi.org/10.1016/j.watres.2019.115229

[32] T. T. H. Van, Z. Yidana, P. M. Smooker, and P. J. Coloe, "Antibiotic use in food animals worldwide, with a focus on Africa: Pluses and minuses," Journal of global antimicrobial resistance, vol. 20, pp. 170-177, 2020.

[33] S. J. Patel, M. Wellington, R. M. Shah, and M. J. Ferreira, "Antibiotic stewardship in food-producing animals: challenges, progress, and opportunities," Clinical therapeutics, vol. 42, no. 9, pp. 1649-1658, 2020. doi.org/10.3390/antibiotics11070867

[34] Z. Akhmet, G. Zhaxylykova, R. Sukor, A. Serikbayeva, and K. Myrzabek, "INCIDENCE OF HORMONAL GROWTH STIMULANT AND ANTIBIOTICS RESIDUES IN CHICKEN MEAT," Slovak Journal of Food Sciences, vol. 15, 2021. DOI: 10.5219/1663

[35] D. C. Rocha, C. da Silva Rocha, D. S. Tavares, S. L. de Morais Calado, and M. P. Gomes, "Veterinary antibiotics and plant physiology: An overview," Science of The Total Environment, vol. 767, p. 144902, 2021. doi: 10.1016/j.scitotenv.2020.144902