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Comprehensive insights into antibiotic residues in livestock products: Distribution, factors, challenges, opportunities, and implications for food safety and public health

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ABSTRACT

From a public health point of view, antimicrobial residues pose various problems, including potential risks for consumers. The use of some of these antibiotics may affect the form and quality of animal products or affect the quality or output of food processing. Consequently, there is a pressing need for further investigation into the effects of antibiotics on animal products. This review endeavors to catalyze collaborative efforts and inform decision-making aimed at safeguarding consumer health, promoting sustainable agriculture, and advancing food safety initiatives in both local and global contexts. These investigations indicate that management practices, such as failure to adhere to withdrawal periods and lack of awareness, among others, may contribute to the presence of antibiotic residues in the environment. Furthermore, different parts of animals, such as the liver, kidneys, and muscles, receive varying doses of antibiotics based on factors like age and hydrophobic or lipophilic properties. Various cooking methods, including roasting, frying, microwaving, and boiling, significantly influence the reduction of antibiotic residues in animal products. However, freezing is found to be one of the least effective methods for eliminating these residues. Additionally, dairy products may retain antibiotics due to processes like curding milk and whey salting and acidification. Implementing proper cooking practices, including multiple heat applications such as combining cooking with frying and subsequent cooking, can help decrease the concentration of antibiotic residues in food products. Therefore, careful attention must be paid to food processing methods to ensure food safety and consumer health.

1. Introduction

Over the last several decades, the animal production system has been inextricably interwoven with numerous societal issues including the public's health. Animal agriculture, in particular, finds itself amid fundamental change and transforming forces (National Research Council, 2005). The potential implications of the global food-animal system and its associated impact on food safety work are without

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precedent. The integration of antibiotics into animal nutrition traces back approximately seven decades to the pioneering work of several researchers (Anonymous, 1952). Since its inception, this practice has evolved to become the linchpin of modern livestock production systems, catalyzing a transformative shift in agricultural practices worldwide. The advent of antibiotic supplementation precipitated a dramatic surge in the domestic livestock population and revolutionized animal nutrition and gut modulation strategies. Moreover, it spurred significant changes in animal management methodologies, reshaping the landscape of livestock farming. In tandem with these advancements, the escalating global demand for animal protein has propelled a transition towards more intensive livestock production systems. These systems rely heavily on antimicrobial agents to uphold animal health, sustain productivity levels, and ensure economic viability within the industry. As such, the historical progression of antibiotic usage in animal nutrition underscores its pivotal role in meeting the burgeoning demands of modern agriculture. Yet, this reliance on antimicrobials also necessitates a nuanced consideration of their implications for animal welfare, public health, and environmental sustainability in the contemporary era.

Approximately 75% of the 12 million kg of antibiotics used worldwide yearly are used to treat infectious diseases, and others are used for preventive or growth promotion purposes (Van Boeckel et al., 2015). This usage has led to many challenges in the livestock food system, one of which is antibiotic residues. These residues occur in all livestock production systems in all countries, albeit at different intensities, and can be found in all animal products (milk, meat, eggs). This still occurs even in countries with regulations and surveillance. The worst-case scenario (exposure to animal products with antibiotic residues and microbial-resistant genes) is expected in many low and middle-income countries where there are few or no regulations and surveillance and where there is indiscriminate sale and high usage of veterinary antimicrobials (Ikhimiukor et al., 2022).

The ban on the use of antibiotic growth promoters by the EU due to microbial-resistant genes was a game-changer in the livestock industry. Since then, nations have followed suit, including China in 2020. This is because of the positive relationship that exists between the intensity of antibiotic use and all associated consequences of antibiotics in animal products and the environment. Despite the ban, many farmers (of all categories and capacities) in many nations still use antibiotics, albeit in different responsible ways (some reckless and some cautious). Due to this use (judicious or indiscriminate), another problem is emerging in the form of antibiotic residue in animal products, which has not been fully addressed in low and middle-income countries. The nutritional benefits of animal products are paramount for consumer health and well-being. However, the presence of veterinary drug residues poses a significant risk, potentially compromising the nutritional quality of these products and, consequently, the health of consumers. Thus, the primary objective of this review is to comprehensively assess the impact of antibiotic residues on consumers, identify sources, and underlying factors contributing to their presence, and propose viable solutions to mitigate this pressing issue. This research will serve as a critical resource for a diverse audience, including farmers, researchers, and consumers, as well as governmental and non-governmental personnel involved in food safety and public health regulation. By elucidating the adverse effects of antibiotic residues on human health and highlighting the complex interplay of factors influencing their occurrence, this review aims to raise awareness and foster informed decision-making among stakeholders. By synthesizing current knowledge and offering actionable insights, this review endeavors to catalyze collaborative efforts and informed decision-making aimed at safeguarding consumer health, promoting sustainable agriculture, and advancing food safety initiatives in both local and global contexts.

2. Materials and methods

A broad-ended search was conducted without language discrimination in English, Arabic, Turkish, and Spanish peer-reviewed work. Articles generated from the initial search were checked manually through abstracts and by extracting information from the full text. The initial search keywords were "antibiotics residue", "antibiotics and poultry", "antibiotics residue and milk", "antibiotic and animal products", "antibiotics in ruminants", and "effects of antibiotics residues", and this was done for domesticated monogastric and ruminants. Databases of Scopus, Science Direct, Google Scholar, Academia, ResearchGate, and Wiley Online were used for the literature search between June 2023 and January 2024. In all, 350 original articles, reviews, chapters, and reports were downloaded, out of which 136 were relevant to this work. Others were excluded due to repetitive ideas, and non-alignment with our aims.

3. Antibiotics/group of antibiotics used on livestock farms

Antibiotics belong to several classes: β-lactam, cephalosporins, chloramphenicol, sulfonamides, macrolides, aminoglycosides, quinolones, fluoroquinolones, lincosamides, tetracyclines. Some of the β-lactam antibiotics include ampicillin, penicillin G, cloxacillin, dicloxacillin, and cephalexin. quinolones such as ciprofloxacin, enrofloxacin, marbofloxacin, danofloxacin, difloxacin, sarafloxacin, flumequin, norfloxacin, flumequine, oxalic acid, and oxolinic acid are approved for usage in animal production (Quintanilla et al., 2019). Others come in the form of oxytetracycline, chlortetracycline, gentamicin, neomycin, streptomycin, sulfadimethoxine, erythromycin, and bacitracin, amoxicillin, sulfamethazine for poultry, swine, ruminants, and pseudo-ruminants and can be applied orally (water or feed), as injectable, transfusion, topically. In Nigeria, various groups of antibiotics are sold, including penicillins (amoxicillin and penicillin G), cephalosporins (cephalexin, ceftiofur); tetracyclines (doxycycline, oxytetracycline), aminoglycosides (gentamicin, amikacin), macrolides (tylosin, erythromycin), fluoroquinolones (enrofloxacin, marbofloxacin), sulfonamides (sulfadiazine, trimethoprim-sulfamethoxazole), and lincosamides (lincomycin). Another issue with antibiotics is their frequent use of broad-spectrum formulations, which combine multiple antibiotics. These are prevalent in developing nations and are found in various forms like liquids, powders, and packaged in sachets, plastic, and glass bottles. They come in diverse colors including brown, white, creams, and dark shades. Despite different brand names, commercialized antibiotics share common active ingredients and consist of a combination of multiple antibiotics in their formulation (Table 1).

4. Distribution of antibiotics in animal products

Literature indicates that antibiotics exhibit non-uniform distribution within animal tissues or products, a phenomenon influenced by tissue distribution during product formation and food processing techniques. The distribution of antibiotics can vary significantly among different components of animal products. For example, in the case of β-lactam drugs, a smaller proportion was observed to transfer from milk to cheese curd (1.6–12.5% of the original amount), with the majority being transferred into whey (33.2–74.1%). Conversely, for non-β-lactam drugs, most were retained in the curd (Giraldo et al., 2017). Similarly,

Table 1
Antibiotics/group of antibiotics used on livestock farms.

Group	Antibiotic
Quinolones	Ciprofloxacin, Enrofloxacin, Marbofloxacin, Danofloxacin, Difloxacin, Sarafloxacin, Norfloxacin, Flumequine,
Penicillins	Amoxicillin and Penicillin G
Cephalosporins	Cephalexin, Ceftiofur
Tetracyclines	Doxycycline, Oxytetracycline
Aminoglycosides	Gentamicin, Amikacin
Macrolides	Tylosin, Erythromycin
Sulfonamides	Sulfadiazine, Trimethoprim-sulfamethoxazole
Lincosamides	Lincomycin

tetracyclines were found to concentrate more in curd and cheese, less in cream and buttermilk, and least in butter and whey (Gajda et al., 2017). These variations in distribution may be attributed to the nature of antibiotics, where lipophilic antibiotics preferentially accumulate in products (cheese, cream, etc.) rather than in milk due to the complexes they form with proteins or fat (Akansale et al., 2019). Residues of certain antibiotics (e.g., ampicillin or penicillin G) were not detected in cheese or whey powder but were found in whey at concentrations similar to those added to raw milk, while others (cloxacillin and dicloxacillin, tetracyclines) were transferred to cheese and whey, concentrating in whey powder (Gianni et al., 2023). This demonstrates that antibiotic class alone is not the sole influencer of the distribution and concentration of residues in animal products, but food processing methods and the specific nature of the antibiotics in question also play a crucial role. Antibiotic groups influence their movement and distribution in different animal production tissues. For instance, a study by Sallam et al. (2022) revealed that the amount of oxytetracycline and tetracycline found in the kidney of sheep was greater in proportion than those found in the liver and muscle. Additionally, the study of amoxicillin and tylosin showed similar variations between muscle, liver, and kidney. Mahmudul Hassan et al. (2021) also found that the liver and kidney contain high residue and the type of animal species influence the antibiotics that may have the highest concentration in a particular organ and the same antibiotics are concentrated in different muscle parts of the same animal. There appears to be a preference for antibiotics to accumulate in livestock visceral organs compared to muscle. The philic or phobic nature of antibiotics can influence their distribution in different regions of muscle, liver, and kidney, possibly due to the distinct metabolic roles of these organs. Radioactive-labeled antibiotics administered through intra-mammary infusions showed an inverse relationship between antibiotic concentration in the cream and the overall product. The interaction of drugs with proteins also affects distribution, with the concentration of drugs in casein usually higher than in whey due to the higher protein content in casein (Virto et al., 2022). Antibiotics' attachment to tissue matrix, expulsion rate, and withdrawal period for each antibiotic differ. In poultry, Yan et al. (2020) found more antibiotics in chicken giblets than in chicken meat and eggs. Khattab et al. (2010) demonstrated that the percentage of egg white samples positive for amoxicillin residues was higher than that of egg yolk samples (Table 2).

Table 2
Distribution of antibiotics in animal products.

Animal product	Antibiotic residues	Effects	Reference/s
Milk	β-lactam drugs	Transfer from milk to cheese curd (1.6–12.5% of the original amount), with the majority being transferred into whey (33.2–74.1%).	Giraldo et al. (2017)
Milk	Non-β-lactam drugs,	Most retained in the curd	Giraldo et al. (2017)
Milk	Tetracyclines	concentrate more in curd and cheese, less in cream and buttermilk, and least in butter and whey	Gajda et al. (2017)
Milk	Ampicillin or penicillin G	Not detected in cheese or whey powder but were found in whey at concentrations similar to those added to raw milk.	Gianni et al. (2023)
Milk	Cloxacillin and dicloxacillin, tetracyclines	Transferred to cheese and whey, concentrating in whey powder	Gianni et al. (2023)
Poultry Tissue	Not specified	More antibiotics in chicken giblets than in chicken meat and eggs.	Yan et al. (2020)
Egg	Amoxicillin residues	The percentage of egg white samples positive for residues was higher than that of egg yolk samples.	Khattab et al. (2010)

5. Other factors influencing antibiotic prevalence or concentration

The presence of antibiotics in animal tissues is contingent upon the specific antibiotics administered and their elimination rates, influenced by factors such as the interval between administration and slaughter. The prevalence of antibiotic residues varies across different livestock species and is shaped by regional antibiotic usage practices (Yamaguchi et al., 2015). Notably, broilers have exhibited a higher incidence of antibiotic residues compared to layers and indigenous chickens (Kabir et al., 2004). Disparities in antibiotic residue levels are apparent in indigenous cattle, with Tanzanian cattle displaying significantly higher oxytetracycline residues in organs compared to Nigerian cattle (Adesokan, Akanbi, Obaweda, Vuuren, & Bogaard, 2015; Kimera et al., 2015). The marked contrast in residue levels between the two countries suggests variations in antibiotic dosages or withdrawal periods. Understanding the route of administration (oral, intramuscular, parenteral, intra-mammary) and drug concentration is crucial in interpreting antibiotic residue levels in animal products (Fathy et al., 2015; Virto et al., 2022). In swine, the disappearance rate of colistin injected intramuscularly varied among tissues, emphasizing the preference for antibiotics for different body tissues (Tang et al., 2009). Variations in antibiotic levels between livestock species may also be attributed to antibiotic properties and animal physiology or structure. For instance, Huong et al. (2020) found more tetracycline residues in chicken and sulfonamide residues in pork. The lipophilic nature of sulfonamides may result in higher retention in pork compared to chicken, indicating the influence of the animal's development system on antibiotic expulsion. Several reports indicate that antibiotics administered to ewes can extend withdrawal periods, highlighting the variability in antibiotic exposure among consumers (Berruga et al., 2003; Molina et al., 2003). This underscores the impact of animal species on drug metabolism and expulsion, emphasizing the importance of a country-specific approach when assessing antibiotic residues. To ensure an accurate interpretation of antibiotic residue levels in animal products, it is essential to account for country-specific practices and variations in antibiotic administration and withdrawal protocols (Fig. 1).

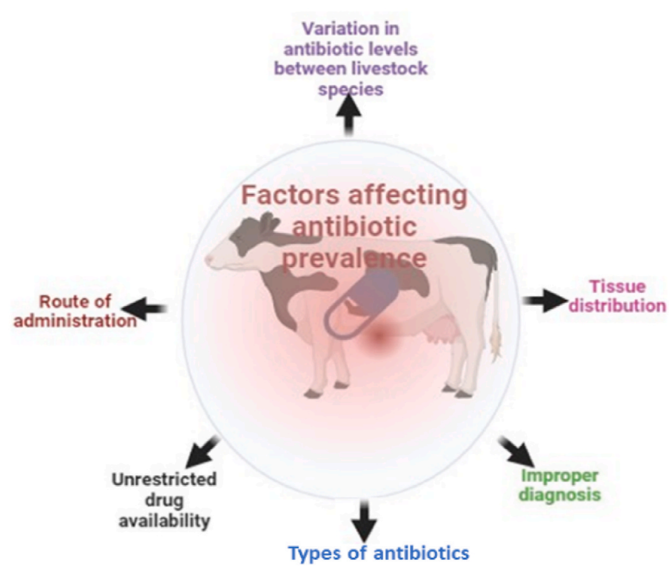

Fig. 1. Different factors affecting the antibiotic prevalence.

6. Physiology/mechanism of distribution of drugs in different meat part

The elevated concentration of antibiotic residues in eggs and milk may be attributed to their association with reproductive systems and mammary tissues. Following intestinal absorption, drugs are transported via blood plasma, leading to their deposition in the yolk in the ovary or egg white in the oviduct. Antibiotic compounds distributed throughout the body, especially in the ovary with growing follicles and the oviduct where egg white is formed and secreted, may increase the likelihood of unacceptable residues in eggs. The physicochemical properties of drugs, hen physiology, and egg formation processes collectively determine the extent of drug deposition (Woodward, 1991). The half-life and stability of antibiotics further influence their distribution in the animal system (Donoghue et al., 1996). Following intra-mammary administration, the distribution of antibiotics is heavily influenced by the lipid solubility of the administered drug and its dissociation constant (pKa). The pKa, which dictates the concentration of the undissociated drug in milk and its transfer rate from milk to blood, plays a pivotal role in this process. Assessing the degree of lipid solubility involves comparing the lipid-to-water partition coefficient (Ko/w), with a higher Ko/w indicating faster drug absorption. Consequently, pKa emerges as a crucial determinant of drug absorption from the udder. Furthermore, certain antibiotics bind to proteins, thereby affecting the absorption rate of the drug (Ziv & Sulman, 1975). A comprehensive understanding of these factors is essential for grasping the intricacies of antibiotic distribution in eggs and milk.

7. Rationale for antibiotic utilization in livestock farming

The exploitation of animals as the foundation of intensive animal production, supporting genetically and nutritionally enhanced livestock systems, has been prevalent in both developing and developed countries. These systems often prioritize overcrowding and engage in numerous unhealthy practices that demonstrate insensitivity to animal welfare. This approach has led to the management of animal stress, overfeeding, overcrowding, mastitis, laminitis, acidosis, microbial dysbiosis, rapid animal growth, and continuous breeding. The modernization of livestock breeds/genetics has increased susceptibility to diseases due to immature immune systems, musculoskeletal problems, heart issues, pain, and respiratory challenges, as their bodies may not be proportioned for efficient respiration and cardiovascular function, especially in broiler chickens and younger livestock. Furthermore, the use of antibiotics has become integral to managing challenges associated with modern animal production. Livestock with not fully developed immune systems, especially during weaning or when fattened to reach market weight, are more susceptible to various diseases, including digestive issues such as ascites and sudden death. Consequently, the complete removal of antibiotics from contemporary animal production systems could significantly impact the livestock industry, potentially reversing some of the gains made in food production. Factors influencing the continued use of antibiotics include the anticipation of disease outbreaks among the flock, swift decision-making based on clinical symptoms like increased mortality, declining performance parameters such as egg and milk yield, and weight gain. In fact, Watt Global Media, (2024) reported increased health challenges such as Coccidiosis, Necrotic enteritis, Colibacillosis, Gengeronous enteristis among others after antibiotics reduction/eminination from poultry. The need to mitigate economic losses and maintain farm profitability is also a driving force (Mdegela et al., 2021). This underscores the complex interplay of economic considerations and animal health in the livestock industry (Fig. 2).

8. Influence of sources of animal products on residue

Generally, in the human system, those who are financially less privileged often afford food of lower quality. This section aims to investigate which market is most exposed or has the highest prevalence of antibiotic residue. Meat from shops in suburban areas was found to have more residues than those from shops in urban districts (Van Nhiem

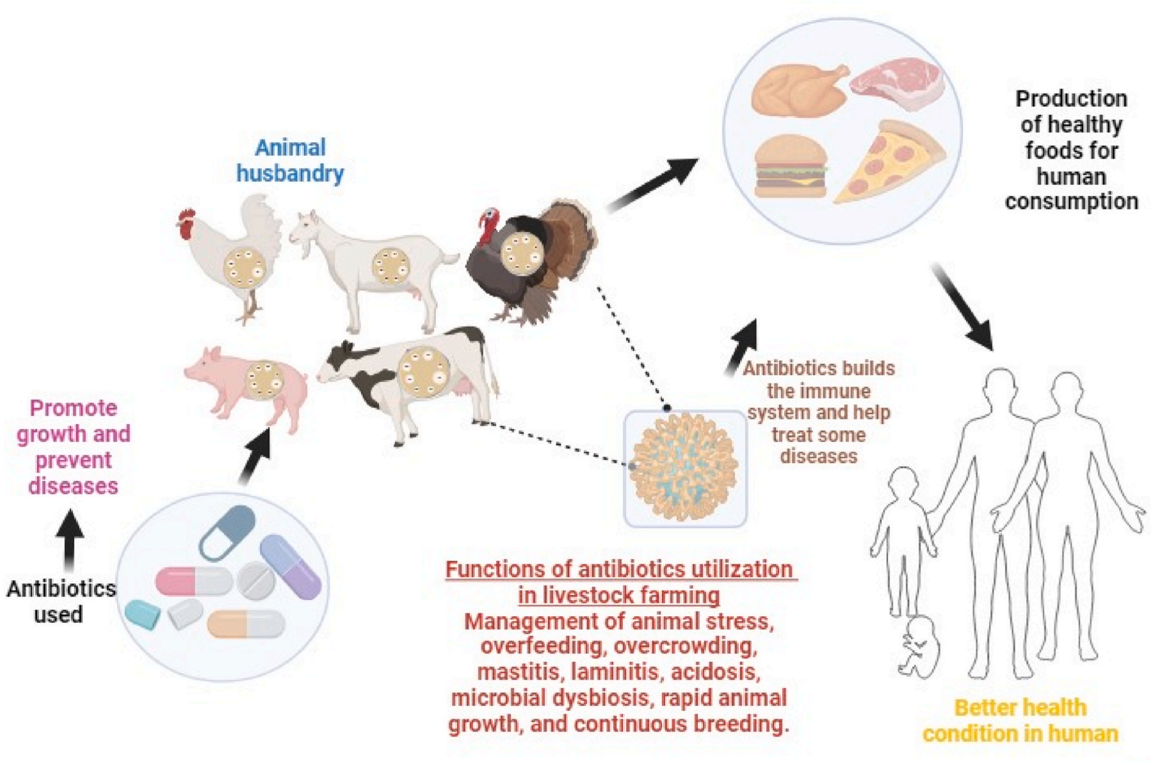

Fig. 2. Antibiotics utilization in livestock farming.

et al., 2006), while meat from wet markets exhibited a higher prevalence of residues than those from supermarkets (Thi Nhung et al., 2018). It was also observed that shops selling raw milk samples had a higher prevalence of antibiotic residue compared to shops where milk is dispensed from automated vending machines (Ouma et al., 2021), possibly influenced by the milk source and certain heat treatments. Pork originating from animals slaughtered in urban abattoirs was found to contain fewer drug residues compared to pork from local abattoirs (Rakotoharinome et al., 2014). This discrepancy may stem from differences in sourcing practices and adherence to standards implemented by the respective slaughterhouses. It is conceivable that urban abattoirs adhere to stricter regulations, possibly employing veterinarians and enforcing higher standards of animal health. In contrast, local abattoirs, subject to less stringent animal health laws, may permit the slaughter of sick animals treated with drugs. The location of animal rearing can also affect the level of antibiotic residue in animal products. Huong et al. (2020) found higher residues in products coming from North and South Vietnam than in central Vietnam. Local chicken and milk contain high levels of antibiotic residue, similar to or even higher than imported meat and industrially packed milk (pasteurization and sterilization) (Mottaghianpour et al., 2018). However, conflicting literature suggests that imported milk has higher antibiotic residue than local milk, while others claim local milk contains more antibiotic residue than imported milk (Redding et al., 2014). One influencing factor in these discrepancies is the method of milk production, the number of days post-withdrawal period the milk was collected, and the country of origin of the imported milk, as different countries have varying standards regarding antibiotic residue levels. Redding et al. (2021, p. P11474) showed that milk sold in the US dairy industry, whether organic or conventional, is essentially antibiotics-free due to adherence to pasteurization ordinances in the industry. Hence, it can be seen that the source of milk can influence the risk of antibiotic residue in animal products. The presence of antibiotics residue in both local and imported products, locally and foreign-produced products, and in local markets and supermarkets shows that both the rich and the poor are not spared from the impact of antibiotic residue.

9. Effect of antibiotics on human consumers

Recent developments emphasize the importance of expanding the emphasis on food security to protect human health and sustainably enhance overall well-being. Although few cases of human antibiotic residue exposure have been documented (Arsène et al., 2022), it is crucial to raise awareness about the potential risks associated with antibiotic residues. Authors like Moudgil et al. (2019) have raised food safety concerns about antibiotic residues above the maximum limit and their health risks to consumers in India. Veterinary drugs were also detected in the urine of preschool children in Hong Kong, which was attributed to food, tap water intake as well as conventional and organic egg intake (Li et al., 2017). Yet, many consumers may be unaware of whether the residues present in the products they purchase are at safe levels or pose a high health risk. The bioaccumulation of residues present in animal tissues and products over individuals' lifespans through prolonged intake may pose a threat to consumers (Cadmus et al., 2006). Diseases resulting from exposure to toxic substances, including drug residues, at concentrations hazardous to humans or other animals, are classified as diseases of toxicological origin (National Research Council, 2005). Antibiotic residues could serve as potential toxicological agents, with exposure being potentially hazardous to humans, particularly affecting children and the economically disadvantaged. Their presence in animal products (meat, milk, and eggs) can induce antimicrobial resistance) (Mahmudul Hassan et al., 2021). Long-term consumption of foods containing excessive veterinary drug residues can lead to acute and chronic poisoning effects, including teratogenic, carcinogenic, and mutagenic effects. Food contaminated with antibiotic residues may cause bone marrow dysfunction, interfere with intestinal flora, and trigger skin allergies to sulfonamides when occurring in high concentrations.

Antibiotic residues found in animal products have the potential to disrupt various bodily systems, including the immune, endocrine, nervous, and reproductive systems, and may contribute to the development of congenital anomalies (Pengyun, Wu, Fang, & Cravotto, 2023). For example, studies conducted on a zebrafish model exposed to raw and pasteurized cow milk containing ceftriaxone residue revealed developmental and genotoxic effects (Chowdhury et al., 2015). Additionally, residues of drugs like quinolones have been shown to inhibit enzymes crucial for DNA replication and transcription, such as DNA gyrase (Suto et al., 1992). Furthermore, degradation products resulting from heat treatments of antibiotics, such as α and β-apo-OTC or Cefaldehyde (derived from Oxytetracycline and ceftiofur, respectively), have been found to induce cytotoxic effects on human lung, liver, and kidney cells (Habeeb et al., 2022). Despite being banned from use, these substances are still being employed in the Latin American ruminant industry, with residues detectable in milk. Ingestion of these ionophore compounds can lead to adverse health effects such as heart problems, kidney failure, and, in severe cases, death (Pressman & Fahim, 1983). Moreover, their presence in milk has the potential to impact its palatability, as evidenced by a study where milk containing the highest levels of contaminants led students to refrain from consuming it due to its undesirable taste, potentially affecting milk sales (Habeeb et al., 2022). Indeed, evidence indicates that the presence of antibiotics in the bloodstream of individuals infected with malaria can elevate the risk of disease transmission and enhance vectorial capacity (Gendrin et al., 2015). In regions where antibiotic residues are consumed through animal products, this phenomenon could potentially exacerbate malaria cases and transmission among the population. Could this be a contributing factor to the prevalence of malaria in developing countries in Africa?

10. Estimated daily intakes and acceptable daily intakes

Exposure to antibiotic residues may be influenced by the frequency with which individuals consume animal protein and their body weight. Some estimated daily intakes (EDI) for antibiotics may present lower values than acceptable daily intakes (ADI), but their long-term presence predisposes consumers to drug resistance and allergic reactions (Hussein et al., 2016). The ADI represents the amount of drug residues that can be safely consumed per day over a human lifetime without adverse effects. Increased availability of animal products may lead to higher consumption and a higher probability of dietary exposure to antimicrobial residues in the long run. Among animal product consumers, the young (children and teenagers) are the most sensitive group, followed by adults. Due to physiological differences compared to adults, children have higher exposure levels per kilogram of body weight, as they have a higher body surface-to-body weight ratio and higher intake of calories and water compared to adults, making them more susceptible to various residues (Kyriakides et al., 2020). The presence of antibiotics in animal products may not necessarily mean a health risk. It was observed that despite the presence of multiple antimicrobial levels, the estimated daily exposure dose was found not to pose a health risk to those above twenty years of age (Kyriakides et al., 2020). However, it can be observed from many studies that low antibiotics EDI and ADI cannot be considered safe because most of these studies usually consider only one animal product, whereas individuals may be exposed to varying sources of animal proteins, such as beef, fish, lamb, milk, and eggs simultaneously. Preference for a specific type of meat can increase the risk of exposure to particular antibiotics, and such preferences can be influenced by socioeconomic factors, age, religion, and monthly income. The mean estimated daily intake of each antibiotic is influenced by age group (adults, children, adolescents, elderly) and sex (males and females) and differs for each antibiotic. The EDI values of antibiotics and anthelmintics via animal product consumption for toddlers and children were three times higher than those for adults, suggesting that toddlers and children experience more exposure, mainly due to lower body weight and a higher volume of animal product intake (Chang et al., 2023). Younger ages are expected to consume more antibiotics, and males are expected to consume more than females (Hoteit et al., 2022).

11. Factor responsible for antibiotics in animal products

11.1. General

Poor adoption and implementation of biosecurity measures on farms expose livestock to diseases and necessitate the continuous use of antibiotics. Non-adherence to withdrawal periods is a common issue, as farmers may sell their animals when facing financial difficulties or to prevent the loss of sick animals to death, leading them to overlook withdrawal periods before selling (Akansale et al., 2019). Harsh economic conditions often allow only a 1-day withdrawal period for animal products, regardless of the antibiotic used (Keyyu et al., 2003). Moreover, the use of broad-spectrum antibiotics, which require strict adherence to individual withdrawal periods for each antibiotic in the combination, can pose challenges. Animals with lower milk production may experience prolonged withdrawal periods after antibiotic therapy (Molina et al., 2003). In tropical regions, forage-fed animals with inadequate diets may grow slowly and produce small amounts of milk, contributing to prolonged withdrawal periods. Broad-spectrum drugs containing a combination of different antibiotics may necessitate extended withdrawal days to ensure the complete expulsion of all antibiotics from animal tissues. The practice of administering drugs beyond the recommended dosage, termed extra-label dosage, can lead to residue presence even if withdrawal periods are adhered to. Often, this practice relies on the "experience" of veterinarians, particularly in regions where drug adulteration is prevalent, prompting extra-label dosing recommendations. If these drugs are lipophilic and heat-resistant, residues may persist unless withdrawal periods are extended. Moreover, seasonal variations significantly impact residue levels, with the lowest detected in the spring season. Antibiotic residues tend to peak in summer and decrease in winter. The intensified use of antibiotics during summer may be attributed to factors such as dehydration due to high temperatures, increased disease prevalence, and malnutrition. Elevated antibiotic residues coincide with warm and humid weather conditions, corresponding to periods when birds are more susceptible to respiratory ailments and diarrhea. Additionally, the antibiotic treatment of both sick and healthy animals contributes to antibiotic residues in animal production. Many orally administered antimicrobials have a low degree of absorption from the gastrointestinal tract, and there is a relationship between peroral antimicrobial use and antibiotic residues in feces, influencing residue levels more than parenteral use (Andersen et al., 2023)- (Fig. 3).

11.2. Influence of management practices on antibiotics use and residue

Various methodologies are utilized in livestock rearing worldwide, shaped by environmental factors, knowledge base, financial resources, socio-economic circumstances, farming scale, traditional practices, cultural norms, and attitudes towards animal welfare. Additionally, the species of animals, stages within the livestock management life cycle, and production phases play a significant role in determining the extent of antibiotic exposure. Research indicates that pigs exhibit the lowest average antimicrobial usage per kilogram of animal produced globally, with chickens following closely behind, while cattle demonstrate the highest usage levels (Van Boeckel et al, 2015). Nevertheless, these usage patterns may vary considerably across continents, countries, and even within specific regions of individual countries. For example, in Southeast Asia, fattening swine has the highest antimicrobial consumption, with a rate of 238 mg/population correction unit compared to 16 mg/population correction unit in broiler chickens (Coyne et al., 2019). This indicates that the demand for animal products influences the exposure of animals to antibiotics.

High animal populations are associated with elevated antimicrobial use. Commercial farms with larger livestock numbers are more responsible for antibiotic residue. Studies by Hoteit et al. (2022) and Chowdhury et al. (2015) observed higher antibiotic use and residues on commercial farms (dairy and layers) with higher numbers of livestock compared to local farms. The prevalence of antibiotics in each species is highly dependent on the production system. Animals reared primarily under intensive systems tend to have higher antibiotic use per kilogram of meat produced. Farm management practices play a crucial role in determining the selection and frequency of antibiotic usage, thereby influencing the presence of antibiotic residues. Domestic animals are typically raised and treated under various farming management schemes. Research indicates a 14% rise in antimicrobial residues in intensively managed farms compared to semi-intensively managed beef farms. Moreover, regardless of whether they are conventional, organic, or antibiotic-free, all production systems exhibit antibiotic contamination, highlighting the pervasive nature of antibiotic residues. Intensive

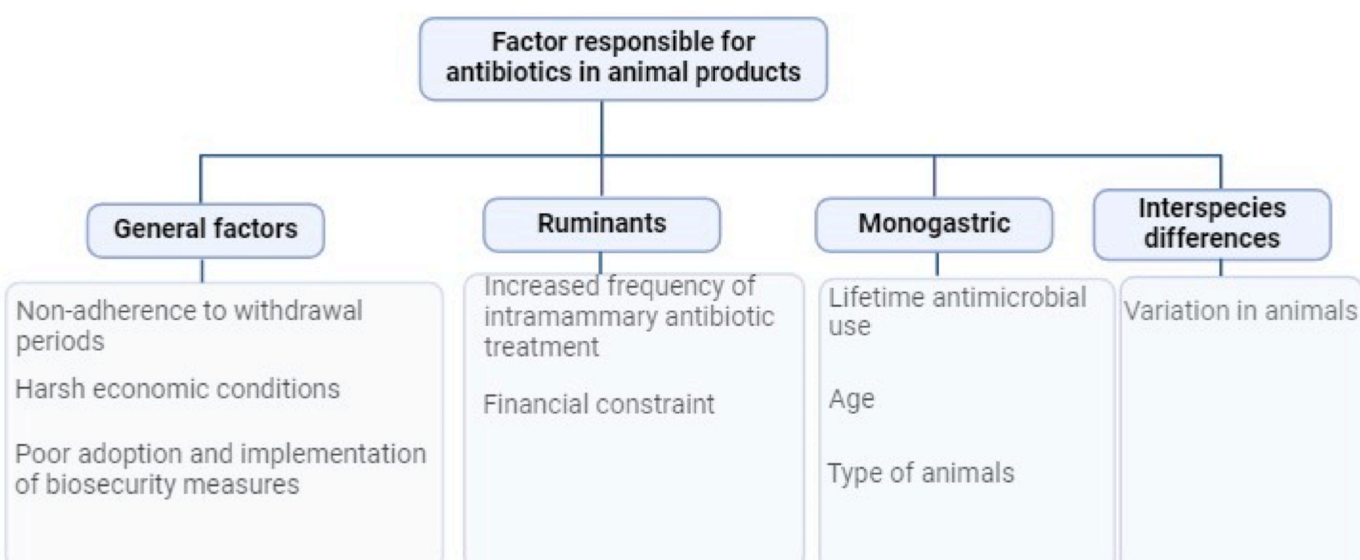

Fig. 3. Summary responsible for antibiotics in animal products.

poultry production systems are categorized into battery cages and deep litter systems. While the deep litter system is recommended as an alternative due to welfare concerns, it favors the accumulation of antibiotics, especially with repeated use of the same litter. This might explain the presence of antibiotics in livestock meat even when the withdrawal period has been observed, given poultry's scavenging tendencies. However, despite repeated use, some antibiotics, like ofloxacin, may undergo microbial degradation. Feces from swine raised in free-range systems were found to contain 99% fewer antibiotic residues compared to intensively farmed swine (Wang et al., 2023). There is a relationship between antibiotic use and the level of antibiotics in feces, as the majority is excreted in the feces when only a small amount is absorbed by the animals (Qiao et al., 2018). A study by Zhang et al. (2021) found the overall concentration of antibiotics to be very low in cattle and sheep raised on grassland grazing.

11.3. Other sources of antibiotics introduction to livestock

The prevailing narrative in the literature often attributes antibiotic residue in animal products to the use of antibiotics in livestock feed or treatment. However, evidence suggests that there might be alternative sources of antibiotic residue. Love et al. (2012) and Dréano et al. (2023) demonstrated the presence and persistence of antibiotics in feathers and the feather meal derived from it can be used in animal feed (swine). Thus, feather meal could be a source of antibiotic residue in swine without the knowledge of the farmers. Rui et al. (2022) demonstrated that eggs from birds raised in a free-range system did not necessarily have lower concentrations of antibiotic residue. No significant difference was found between eggs from birds in free-range natural pastures and those in cages. Similar observations were made in backyard production systems where eggs contained more diverse classes of antibiotics compared to intensive systems (Cornejo et al., 2020). Antibiotics have been detected in quail and pheasant eggs, indicating that even game bird enthusiasts are not exempt from antibiotic contamination. Direct contact of pheasants with a contaminated environment, possibly through water sources, might explain the presence of antibiotics in pheasant eggs. Game birds could come in contact with watercourses contaminated with antibiotics due to their proximity to other farms. Reports indicate antibiotic contamination in lake water, wastewater treatment plant effluent, surface water, and groundwater near livestock farms with variable concentrations detected in surface water (Valverde et al., 2006).) This suggests that game birds and extensively reared birds in such areas, even without direct antibiotic treatment, may have residues in their meat. Another potential source could be crops or forages irrigated with wastewater. Crops irrigated with poorly managed wastewater or manure can introduce antibiotics to forage-consuming livestock. The feeding of crop by-products from farms using antibiotics in manure or wastewater can reintroduce antibiotics to animals. Antibiotics are taken up by plants, with different preferences for distribution in the plant body. Tetracycline, fluoroquinolones, and chloramphenicol are more distributed in fruit > leaf/shoot > root, while sulfonamide and macrolide show the opposite trend (Pan & Chu, 2017). The type of antibiotics present in the water will influence where they concentrate. Therefore, it is crucial to avoid using wastewater from livestock farms to irrigate crops intended for animal feed or human consumption. The uptake of antibiotics in crops was higher with wastewater use compared to manure fertilization, and it was suggested that composting and anaerobic digestion are effective methods to degrade and remove antibiotics before applying manure.

11.4. Animal class

11.4.1. Ruminant

In ruminants, the increased frequency of intramammary antibiotic treatment on farms to address mastitis can potentially lead to milk residue problems due to the high concentrations of antibiotics injected directly into the mammary gland (Huong et al., 2020). The susceptibility to diseases and the necessity for antibiotic use may vary among animal species. Warsma et al. (2020) found no antibiotic residues in both goat and camel milk, while 40% of cow milk samples tested positive. Mixing milk from different sources before sale could potentially contaminate "antibiotic-free" milk. Unscrupulous sellers might also add antibiotics to the milk before sale to prolong its shelf life (Ahmed et al., 2008). Financial considerations may drive the conversion of contaminated milk into cheese to avoid discarding it during the withdrawal period (Dankar et al., 2022). However, there is evidence that even in animals with no recent history of antibiotic administration over the last three months or more, antibiotic residues above Maximum Residue Limits (MRL) have been detected. This suggests that either the drugs required more withdrawal time due to extra-label dosing or other sources, such as the drinking water source on the farm or water used in the milking parlor, may be contaminated.

11.4.2. Monogastric

The production cycle that animals go through before final slaughtering determines their exposure levels to antibiotics. Lifetime antimicrobial use (AMU) in swine indicates that AMU is high and prevalent during the early life stages but not as significant during the later stages of the lifetime (Andersen et al., 2023). Sows go through multiple production cycles, including mating, gestation, and farrowing, while piglets have a shorter period before reaching slaughter weight. Consequently, slaughtering weaners and young pigs may contribute to residues in pork, particularly in farms where oral antibiotics are used for extended periods (Alban et al., 2023). The age and type of animal slaughtered also influence residue levels. Sows pose a higher risk of residues compared to finishing pigs, with up to a 20-fold higher prevalence of residues (Baptista, Alban, Olsen, & Petersen, 2010). This elevated risk is attributed to the prolonged exposure of sows to antibiotic use throughout their lifetime, and there is no well-defined time for slaughter. Broilers, due to their short-cycle production system, overcrowding, and less efficient digestive systems, may also accumulate significant antibiotic residues.

11.4.3. Interspecies differences

Variation in animal species can significantly influence antibiotic residues. Studies have shown that antibiotics in ewes could lead to a prolonged withdrawal period (Berruga et al., 2003). Additionally, research by Pengov and Kirbis (2009) demonstrated that the withdrawal period recommended for ewes' milk is longer than that for bovine milk, even when the same antibiotics are administered. Therefore, generalizing withdrawal periods can result in antibiotic residues. The choice of animal species raised in a particular area or the preference for specific animal products in certain regions will impact the prevalence of antibiotic residues. The shorter production cycle observed in monogastric animals might lead to higher residue levels compared to other ruminant species intended for meat. Fattened ruminant species may contain fewer antibiotics compared to dairy ruminant species. The short production cycle of poultry, especially broilers, might affect their ability to eliminate antibiotics effectively due to their still-developing functional systems.

12. Alleviation methods to prevent or manage antibiotics in food

Food safety is becoming a growing global concern due to its direct impact on human health. In many low- and middle-income countries, the issue of food safety initially emerged on their development agendas as a trade and market access concern (Henson et al., 2023). Food processing methods are essential in improving food safety across all antibiotic categories, and it's noted that heat-resistant residues have the lowest safety margins in animal products. Ensuring access to safe food is a fundamental aspect of the food system, and there is a lack of adequate available indicators for food safety. Safeguarding human health is one of the three primary goals of the food system (Table 3).

12.1. Treatment to reduce antibiotic residues

12.1.1. Heat treatment

The presence of multiple members of an antibiotic group, such as quinolones (enrofloxacin, ciprofloxacin, norfloxacin, flumequine, and oxalic acid), in an animal product may impact the efficiency of heat treatments or food processing, even if these methods can degrade them individually (Quintanilla et al., 2019). Different processing steps (pressing, salting, boiling cheeses, acidification of whey) and various thermal treatments, such as pasteurization (72 °C for 15 s and 63 °C for 30 min), resulted in the degradation of 52%–99% of enrofloxacin concentration. Antibiotics like enrofloxacin are highly sensitive to destruction when subjected to higher temperatures for shorter durations (Hassan et al., 2021). However, the tissue subjected to heat will influence the effectiveness of reducing residue, with boiling reducing residue the most in muscle, while roasting reduced oxytetracycline the most in the liver (Vivienne et al., 2018). The effectiveness of heating methods can be influenced by the type of antibiotics used. For instance, frying and grilling reduced oxytetracycline levels by 91–95%, whereas the reduction in residues of enrofloxacin was lower, ranging from 25.6% to 33.3% with the same heating methods (Marouf & Bazalou, 2005). Cooking temperature, method, and time play a significant role in depleting drug residues. Cooking by simmering reduced antibiotics of the tetracycline family up to 86–89% in chilled broiler carcasses, ensuring consumer safety for broiler chicken meat (Shaheen et al., 2022). Long-time cooking at low temperatures, such as simmering, is considered an effective method for reducing antibiotic residues in chicken meat before consumption (Fathy et al., 2015). Microwaving for 1 min was found to reduce TC residue in pork by up to 67% (Hue Nguyen, Li, Khan, Li, & Zhou, 2013). The response of different meat types (pork, beef, lamb, and chicken) to the same drug under the same heating conditions suggests that the matrix and complexes that drugs form with meat depend not only on the rate of antibiotic use but also on the animal species itself. The anatomy of animal species' meat will influence their response to heat treatment (Wu et al., 2022). The form of meat at the time of heat treatment also affects the loss of antibiotics, with minced meat showing a higher rate of loss compared to fresh or kebab meat when subjected to boiling and roasting (Wali & Al Deri, 2022).

12.1.2. Cool temperature

The impact of low temperatures on food processing can vary depending on several factors, including the degree of freezing, duration, animal source, and the type of antibiotic residue present. Literature on this topic presents a mixed picture. For example, freezing at −10 °C for up to 9 days did not significantly affect the concentration of oxytetracycline (OTC) (Vivienne et al., 2018). Chilling meat at 4 °C for 3 days led to a slight decrease in antibiotic residues, approximately 16%, while freezing the meat at −18 °C for six weeks had minimal impact. The duration of freezing also plays a role, with varying effects observed over different periods. Freezing rabbit meat at −20 °C for 12 months resulted in the complete removal of ciprofloxacin but only a 30% reduction in oxytetracycline residues (Shaltout et al., 2019). These findings underscore the complex relationship between temperature, duration, and antibiotic reduction in food processing.

12.2. Degradation products of heat processing

Despite the numerous reports on the benefits of heat treatment in reducing antibiotic residue in animal products, it's crucial to note that residues can be converted from one form to another. Therefore, further care must be taken regarding the health implications of animal products whose residues have been reduced. Heat treatments have been shown to lead to a significant increase in the amounts of degradation products. By-products/degradation products of heat treatments of Oxytetracycline, such as 4-epioxytetracycline or α- or β-apo-OTC, or cefaldehyde – a degradation product of ceftiofur, have been found to cause cytotoxicity to human lungs, liver, and kidney cells (Habeeb et al., 2022). These degradation products may combine with the food matrix, such as the thermal degradation product of ciprofloxacin combined with lactose in milk during heating. Planche et al. (2022) showed that there was up to a 45% antimicrobial loss for sulfamethoxazole. Despite this loss, six degradation products of 14C-sulfamethoxazole were detected in cooked meat.

Table 3
Summary of alleviation methods of reducing antibiotics.

Alleviation methods	Product	Effect	Antibiotics	References
Temperature				
Heat treatment/food processing Pasteurization	Milk	Different processing steps (pressing, salting, boiling cheeses, acidification of whey) and Pasteurization (72 °C for 15 s and 63 °C for 30 min), resulted in the degradation of 52–99%	Enrofloxacin	Hassan et al. (2021)
Boiling and roasting	Animal Tissue	Boiling reduced residue in muscle, while roasting reduced it the most in the liver	Oxytetracylcine	Vivienne et al. (2018)
frying and grilling,	Not specified	frying and grilling reduced oxytetracycline levels by 91–95%, whereas the reduction in residues of enrofloxacin was lower, ranging from 25.6% to 33.3% with the same heating methods	Oxytetracycline; Enrofloxacin	Marouf and Bazalou (2005)
Simmering	Broiler chicken meat	Cooking by simmering reduced antibiotics of the tetracycline family up to 86–89% in chilled broiler carcasses	Tetracycline	Shaheen et al. (2022)
Microwaving	Pork	Microwaving for 1 min was found to reduce TC residue in pork by up to 67%	Tetracycline	Hue Nguyen et al. (2013)
Freezing	Not specified	Freezing at −10 °C for up to 9 days did not significantly affect the concentration of antibiotic residue	oxytetracycline	Vivienne et al. (2018).
Chilling		Chilling meat at 4 °C for 3 days led to a slight decrease in antibiotic residues, approximately 16%, while freezing the meat at −18 °C for six weeks had minimal impact.		Vivienne et al. (2018)
Freezing	Rabbit meat	Freezing rabbit meat at −20 °C for 12 months resulted in the complete removal of ciprofloxacin but only a 30% reduction in oxytetracycline residues	Oxytetracycline, ciprofloxacin	Shaltout et al. (2019)
Food processing	Milk	Curding was found to increase antibiotic concentration by 3.5 times while acidifying or boiling whey into double cream increased it by 1.9 times	Not Specified	Hassan et al. (2021)
Food processing	Milk	Increased by 5 times in the curd of cheese, with only a small amount lost in the whey	Monesin	Nogueira Silva et al. (2020)
Food processing	Milk	Skimming milk was able to remove enrofloxacin by 95%	Enrofloxacin	Hassan et al. (2021)

12.3. Processes that can increase antibiotic concentration

Due to the heat sensitivity of antibiotics, differences in animal tissues, and the varied influence of heat sources on water loss, it has been observed that certain treatments and food processing methods may increase antibiotic residue rather than reduce it. For instance, curding was found to increase antibiotic concentration by 3.5 times, while acidifying or boiling whey into double cream increased it by 1.9 times (Hassan et al., 2021). Monesin in milk was observed to increase by 5 times in the curd of cheese, with only a small amount lost in whey due to its lipophilicity (Nogueira Silva et al., 2020). The lipophilic nature of enrofloxacin and tylosin, for example, makes them soluble in the fat layer, leading to an increase in antibiotics when curding milk and processing whey into cheese. The types of cheeses produced from the same milk can also affect their ability to reduce residue. The retention of antibiotics in cheese depends on the solubility characteristics of these substances and their interactions with the fat and/or protein fraction of the matrix. Cheese manufacture can lead to a concentration of the main milk components (fat and protein), influencing the antibiotic residues potentially present in milk (Quintanilla et al., 2021). Analyzing only the final animal products is not sufficient; it is crucial to understand the influence of each step in the process on the residues, considering that antibiotics belong to different classes with a variety of physical and chemical properties (Hassan et al., 2021). Antibiotics like Florfenicol may increase dairy products such as cheese or milk powder when milk is used in their production because they are not as affected by food processing heat. This may be due to their lipophilic nature, allowing them to penetrate tissues effectively.

12.4. Non heat treatment/food processing

While there are concerns about the potential impact of antibiotic residue on consumers, food processing methods can contribute to improving food safety, even if they may not entirely prevent the transfer of all antibiotics to consumers (Quintanilla et al., 2021). Cheese making, for instance, has been shown to enhance food safety for various categories of antibiotics, including β-Lactams, aminoglycosides, quinolones, and tetracycline. The retention of antibiotics in cheeses varies during ripening, with some antibiotics like enrofloxacin persisting in ripened cheese for months, while others, such as oxytetracycline in ovine milk, decrease during ripening (Cabizza et al., 2017; Quintanilla et al., 2021). This highlights that the type of antibiotic, its interaction with the animal product matrix, and the type of milk can influence its duration in animal products during food processing, particularly for highly stable substances like quinolones. Certain processing methods, such as skimming milk from full-fat milk, have proven effective in reducing antibiotic residues. Skimming milk, for example, was able to remove enrofloxacin by 95% as it was present in the upper fatty layer of the milk (Hassan et al., 2021). Irradiation is another method that has demonstrated effectiveness in reducing antibiotic residue in chicken products. Studies have found irradiation (7 kGy) to be more efficient in this regard (Heydarian et al., 2023). Irradiation involves passing a beam of electrons and gamma rays through the sample to decontaminate it, converting non-degradable persistent organic contaminants into degradable products. This process creates hydroxyl radicals that bind to antibiotics, leading to their destruction and decomposition. Therefore, irradiation can be used to remediate chicken products before export to other nations. Adsorption stands out as a highly effective method for mitigating antibiotic contamination, and biochar emerges as a cost-efficient and chemically inert material suitable for this purpose in milk decontamination. The adsorption capacity of biochar hinges on factors such as biomass source and the pyrolysis process, which shape its surface area, surface functional groups, and porosity. Research indicates that biochar with smaller particle sizes and produced at higher temperatures outperforms alternative materials like activated carbons, carbon nanotubes, clays, and zeolites, demonstrating superior antibiotic removal from contaminated milk samples (Devakumari, 2021). However, the efficacy of the adsorption process is contingent upon the specific antibiotics and adsorbents utilized (Pengyun et al., 2023). These findings underscore the importance of considering various factors in selecting appropriate adsorbents for combating antibiotic contamination in milk.

13. Recommend practices to reduce antibiotics

13.1. Management

13.1.1. Farm

Pre-slaughter actions are crucial in preventing the presence of residues in animal products (Codex Alimentarius, 2014). The European Union (EU) recommends the judicious use of antimicrobials with prescriptions by veterinarians, including appropriate recommendations regarding the withdrawal period before animals are sent for slaughter, to limit residues in agri-food goods (EU Commission, 2017). Maintaining good hygiene and proper biosecurity on farms is another essential practice to avoid infections and reduce the need for antibiotics. Hygiene deficiencies in animal protein production systems may lead to antibiotic use and the presence of antimicrobial drug residues, posing undesirable human health hazards (Thi Nhung et al., 2018).

Effective communication between the animal health officer treating the animal and the person sending the animal for slaughter is vital on farms (Alban et al., 2014). Miscommunication between them can result in the slaughter of animals that have not observed an adequate withdrawal period. Animals treated with drugs should be marked by the primary producer or animal health personnel to prevent unacceptable levels of residues from reaching consumers. Alternatively, separating treated animals into a distinct pen may suffice to prevent mixing (Alban et al., 2023). Considering the presence of antibiotics residue in the mutton of lambs born to ewes given antibiotics postpartum (Testa et al., 2007), it is advisable to avoid treating lactating mothers with antibiotics if their young are slated for slaughter in a short period. Farmers should pay attention to avoiding the use of antibiotics in dams feeding the young that will be slaughtered. Alternatively, bucket feeding milk, especially from dams currently not undergoing antibiotic therapy, may be applied.

Antibiotics administered parenterally are excreted relatively faster through milk compared to intramammary administration, where residues stay the longest and in the highest concentrations (Samaržija & Antunac, 2002). In lactating cows, the parenteral method can be preferred, especially for lipophilic antibiotics. Alternatively, the first milk collected after antibiotic administration should be discarded since about 70%–80% of the drug is found in the first milking after administration (Anifantakis, 1982). Milk should be withdrawn and discarded from all quarters following intramammary infusion of antibiotics, as infused drugs can be disseminated through circulation easily (Beyene, 2016). To reduce mastitis in dairy herds, the use of teat dip is associated with a reduced risk of antibiotic residues, as it minimizes the need to treat animals and lowers the probability of antibiotic residues occurring (McEwen et al., 1991). Additionally, shortening dry cow treatment with an intramammary antibiotic is recommended to reduce the risk of mastitis at the beginning of the next lactation, as observed in Fischer-Tenhagen et al. (2023) study, where cloxacillin benzathine given between 14 and 28 days to parturition fell to MRL levels by the 5th-day post-calving or day in milk, thereby reducing the risk of exceeding MRL.

13.1.2. Non-farm

In developing countries with unregulated food production systems, a crucial aspect of monitoring the value chain involves overseeing commercial feed producers. These producers often tout their feeds as superior, attributing success to additives like antibiotics. Therefore, governments or NGOs need to target these producers and advocate for the judicious use of antibiotics. Drug sellers or dealers also wield significant influence in the production cycle's risk management, impacting farmers' decisions on antibiotic use. Implementing broad or systemic strategies, as suggested by Lam et al. (2017), can be effective. The RESET method, which entails establishing rules and regulations, educating and disseminating information, applying social pressure, considering economic factors, and deploying tools, has shown promising results in the Netherlands. Education, particularly raising awareness about antibiotic dangers and providing training on good milk practices, can significantly reduce antimicrobial residues in milk (Ondieki et al., 2017). Educating farmers on antibiotic risks and enforcing penalties for selling contaminated milk by milk companies are critical for improving milk quality and promoting a food safety culture (Redding et al., 2021, p. P11474). Farmers should understand the need to discard milk from cows treated with certain antibiotics, with severe penalties for violations. Structural changes, such as the implementation of agricultural extension services, farmer support programs, farm treatment, and health plans, and the establishment of task forces involving relevant stakeholders, as seen in the Pasteurized Milk Ordinance in the dairy industry in the US, can positively contribute to reducing antibiotic use and combating antimicrobial resistance (Jimenez et al., 2023).

13.2. Use of supplement/additives: supplemental management to reduce antibiotic residues

Therefore, it appears likely that the ban on antimicrobial growth promoters will impact the overall productivity of the livestock sector. Consequently, producers must receive adequate support in exploring alternative management approaches for disease prevention. The prohibition of antibiotic growth promoters has increased the demand for therapeutic purposes, leading to the exploration of alternatives such as herbal antimicrobial substances, organic acids (acetic acid, formic acid, butyric acid, and propionic acid), amino acids, enzymes, and probiotics as substitutes for chemical antibiotics. Microbes have shown promise as in-feed antibiotic replacements, indicating potential future applications.

The removal of antibiotics from feed has been accompanied by improvements in livestock productivity through the use of various feed additives, including omega-3, immunoglobulin, microalgae, yeast-derived β-glucans, essential oils, prebiotics, probiotics, herbs, and spices. Research conducted on the use of pawpaw, black cumin, and mustard seed as growth promoters, along with gut microbe management, demonstrated their potential in broiler production (Adegbeye et al., 2020a). The adoption of ethno-veterinary science and practices to combat infectious diseases in livestock has resulted in a reduction in antibiotic use. Cows treated with ethno-veterinary practices exhibited decreased incidences of mastitis, enteritis, repeat breeding, and cowpox. Approximately 87.86% of 220 farmers reported a reduction in antibiotic residue incidence in milk one year after implementing ethno-veterinary practices (Balakrishnan et al., 2022). Further research is needed to explore the potential health benefits of fodder and nutraceuticals in local and traditional ethno-veterinary practices (Vogl et al., 2016). Plants known for their significant medicinal properties, attributed to bioactive compounds, should undergo phytochemical and pharmacological validation in the future. This validation process is essential for the development of new alternative drugs for veterinary purposes.

14. Gaps noticed on antibiotic residues

Many studies on meat, including those conducted under controlled environments, often omit the sex of the animals they consider. However, it is crucial to include this information because Greenblatt et al. (2014) have demonstrated gender differences in drug metabolism. Soldin and Mattison (2009) also reported that, due to pharmacokinetics, drugs may remain in the female body longer than in the male body. In studies carried out in milk, particularly those involving starter cultures and yogurt making, there is a need for antibiotic residue tests to be conducted. The authenticity of the reports can be compromised if the same milk obtained from the same herd is used for yogurt with a starter culture, as the presence of antibiotic residues from a herd can affect performance. These differences might be attributed to the influence of various microbes or even the genetics of the animal, without recognizing the influence of other factors such as antibiotic residues. It's essential to mention the origin of milk used for antibiotic residue research in publications to prevent generalized statements like "international source." Our review indicates that some countries, like the US, have thresholds for antibiotic residues regardless of the production system (organic or conventional), while other countries may not. The fact that different organs have varying concentrations of antibiotics necessitates the need for authors to investigate different muscles in the same animal.

The age of the animal from which milk, meat, and eggs are collected needs to be specified in publications. The age of the animal affects clearance, dosage, and production activity, which in turn affects the clearance of residues in animals. Younger animals may not clear residues as effectively as older animals (Adesokan, Akanbi, Obaweda, Vuuren, & Bogaard, 2015). Additionally, there's a need to carry out tests on antibiotic residue consumption under home conditions or even in true restaurant settings. While laboratory experiments are valuable in determining Estimated Daily Intake (EDI) or Acceptable Daily Intake (ADI) of animal products consumed and the associated human risk, real-life scenarios demonstrate that animal products, like meat, might undergo different temperature and processing stages before consumption. For example, when meat is purchased from the market, it might be refrigerated or frozen for some days. Subsequently, the meat may be cut into small pieces, cooked or steamed for about 40 min or more with other condiments, and then fried with hot vegetable oil or smoked. Later, individuals might cook the meat with pepper or other soup ingredients and repeatedly boil the meat for days before finishing the soup. Therefore, it is evident that such meat has undergone various temperature changes and processes which might affect its risks. These aspects are often not considered in laboratory experiments when calculating EDIs and ADIs. To avoid scientists being labeled alarmists, it is essential that research is conducted in this area.

15. Conclusion

In conclusion, our examination of antimicrobial residues in animal products reveals multifaceted challenges and opportunities for safeguarding public health and promoting sustainable agricultural practices. The implications of these residues extend beyond mere contamination, encompassing potential health risks for consumers and the concerning emergence of antimicrobial resistance.

Our analysis sheds light on the diverse factors influencing the prevalence of antimicrobial residues, ranging from management practices and antibiotic characteristics to food processing methods. Notably, the intricate interplay between these factors underscores the complexity of mitigating residue levels effectively. We emphasize the critical role of informed antibiotic usage and stringent adherence to withdrawal periods in minimizing environmental contamination and ensuring food safety. Additionally, our findings underscore the necessity of tailored food processing techniques to mitigate residue levels effectively, particularly in dairy products where residual antibiotics may persist due to inherent processing methods. Looking ahead, collaborative efforts among researchers, industry stakeholders, and policymakers are imperative to address this pressing issue comprehensively. By fostering interdisciplinary collaboration and promoting consumer awareness, we can advance strategies to reduce antimicrobial residues in animal products while safeguarding public health and preserving the efficacy of antimicrobial agents. In summary, our study underscores the urgency of proactive measures to address antimicrobial residues in animal products, advocating for holistic approaches that prioritize food safety, environmental sustainability, and the well-being of consumers and communities alike.

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CRediT authorship contribution statement

Moyosore Joseph Adegbeye: Conceptualization, writing – initial draft and editing, Babatunde Oluwafemi Adetuyi- drew images, writing – review and editing, Anem I. Igirigi - conceptualization, Valiollah Palangi: Writing- editing, Susanna Aiyedun, Ofelia Márquez Molina: – writing- editing, Abosede Adisa, Mona M.M.Y. Elghandour – writing- and editing, Abdelfattah Z.M. Salem, Edwin Rafael Alvarado-Ramírez: writing – review and editing, Abiodun A. Oladipo - editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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