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| RESEARCH ARTICLE

Antibiotic Residue in Milk and Meat Products: A Scientific Overview

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| ABSTRACT

The need for food is rising globally as the human population continues to rise. People in better socioeconomic countries have a tendency to substitute meat and high quality items for grains in their diets. Over the past thirty years, there has been a seventy percent increase in their choice of chicken as a protein source. Antibiotics accumulate in animal tissues as a result of overuse and misuse in treating illnesses and fostering animal growth. From there, they enter human bodies through the food chain. This study provides a detailed assessment of comparative studies on the dangers to human health posed by antibiotic residue (AR) in foods, including milk and meat from animal sources. The usage of several veterinary antibiotics in animal farms, which can result in ARs, is the main topic of this review's early section. Later on, there has been a thorough discussion of ARs in dietary items, such as milk and meat. People from underdeveloped and impoverished nations are particularly susceptible to infectious diseases brought on by bacteria that are resistant to antibiotics, according to review research on the problems with antibiotic use and human health. Towards the conclusion of the review, a few alternative strategies are outlined, taking into account their potential exposure to substitute antibiotics as growth promoters and reducing the prevalence of antibiotic resistant genes. These strategies include the use of probiotics, prebiotics, organic acids, phytogenic feed additives, and other substances.

| KEYWORDS

Antibiotic Residue; Antibiotic Residue in Milk and Meat; Resistant Bacteria; Toxicity

| ARTICLE INFORMATION

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1. Introduction

The need for food is rising globally as the human population continues to rise. People in better economic countries have a tendency to replace meat and high quality items with grains in their diets. Over the past three decades, the demand for chicken as a source of protein has climbed by 70% (Kalia et al., 2022).

Antibiotics are substances that are semi synthetic, synthetic, or naturally occurring that have antibacterial properties and can be applied topically, parenterally, or orally. They are used to promote growth in food animals and to cure and prevent illnesses in both human and veterinary medicine (Laven et al., 2012). However, using them may affect people's health both directly and indirectly (Ngangom et al., 2019).

Indirect impacts come from the use of antibiotics in food animals, which causes resistant organisms to spread to different sections of the environment, like soil and water. Direct consequences come from interaction with antibiotic resistant bacteria in food animals. Antibiotic residues in food derived from animals raise concerns since they may provide a direct hazard to humans and may change the microbiota, leading to illness and the emergence of resistant strains that could undermine antibiotic therapy (Bilandžić et al., 2011).

Antibiotic residues are the result of the widespread use of antibiotics in animal husbandry. They are very small amounts that remain in food products generated from animals. Antibiotic residues can be found in food (milk, meat, and eggs) for a number of reasons, such as inappropriate use of antibiotics, inadequate withdrawal times, and incomplete animal metabolism. These residues are a cause for concern due to potential adverse effects on humans and the emergence of antibiotic resistance in microbes (Van et al., 2020). Bacteria that are exposed to low concentrations of antibiotics for a long period of time may become resistant to them (Treiber & Beranek-Knauer, 2021).

To ensure food safety and stop the spread of antibiotic resistance, it is essential to monitor and regulate the level of antibiotic residues in food items. Regulatory organizations, including the US Food and Drug Administration (FDA) and other comparable organizations across the world, set maximum residue limits (MRLs) for specific antibiotics in different food products. These limitations are in place to enable the proper application of antibiotics in livestock production while reducing the possibility of adverse effects on human health (Booth et al., 2020). In order to maintain antibiotic residues in food below set safety criteria and to ensure compliance with regulations, frequent testing and surveillance programs, together with consumer awareness and education, are essential (Chiesa et al., 2020).

It has been found that not all antibiotics can be absorbed by animals and that between 30 and 90 percent of veterinary medicines can enter the marine ecosystem through wastewater effluent, faces, and urine (Gao et al., 2012; Naquin et al., 2015).

Currently, one of the hazardous pollutants in marine ecosystems, which includes marine life, is veterinary AR. Tetracycline, quinolones, streptomycin, and lincomycin are among the many antibiotics commonly found in milk, tissue, and marine animals and used in farm animals (Redwan Haque et al., 2023). Globally, there is a growing concern for public health regarding AR in animals raised for food. One of the main causes of toxicity, allergic reactions, cancer risk, and the development of bacteria resistant to antibiotics is AR in food (Aguilera-Luiz et al., 2013). On the other hand, multidrug resistant bacteria pose a threat to health because they can enter the human body from a variety of environmental contexts, including animal farm waste, sewage treatment effluent, and aquatic environments (Woolhouse et al., 2015). Antibiotic-resistant disorders are thought to be the cause of about 50,000 deaths per year in the US and Europe (Hargreaves et al., 2017).

2. Veterinary antibiotics used in animal farms

Antibiotics have been used for better growth promotion in food-producing animals, including poultry, for over 70 years (Castanon, 2007). However, due to increased antibiotic resistance in food animals, the European Union completely banned the use of antibiotic growth promoters (AGPs) in animal feed in 2006 (Stolker et al., 2007), and the FDA later requested the voluntary removal of medically important AGPs from animal feed in the United States (Thanner et al., 2016). Additionally, despite the years of using antibiotics as growth promoters, no consensus regarding the mechanism of action of AGPs was ever described based on scientific evidence (Miyakawa et al., 2024).

China produced 248 thousand tons of antibiotics in 2013, 52% of which were used in the treatment of cattle, indicating a significantly larger use of antibiotics in China than in developed countries. China has an average daily dosage of 157 g per 1000 people, which is significantly higher than that of the US, UK, Canada, or Europe. China exceeds the US by 2.8 times when it comes to the amount of animal antibiotic use. Antibiotics make up more than half of the top 100 medications sold in China; none are listed in either Europe or the US. According to WHO data, 70% of antibiotics used worldwide are used in Asia, with 70% of those uses occurring in China.

According to Lyu et al. (2020), there is extensive antibiotic contamination in China, especially along Bohai Bay. The two main types of contaminants in soil are quinolones and tetracyclines. Antibiotic concentrations in Chinese rivers are significantly higher than those in American, German, and Italian rivers, according to a 2015 survey. The abuse of antibiotics has become a serious cause of pollution to the environment and a health hazard to people, so immediate regulations and reduction measures are required (Zheng et al., 2021).

Antimicrobial drugs have been used in livestock production since the early 1950s to treat disease, promote growth, and increase feed efficiency. Prior to the growth promoter ban in Europe, it is estimated that the majority of antibiotics used in agricultural livestock production were given to pigs and poultry, with only 1% of prescriptions going to other species (Kemper, 2008; Ungemach et al., 2006).

Antibiotics work effectively to cure bacterially caused infectious disorders, but they are ineffective against viruses and fungi. Since chickens fed pharmaceutical wastes containing aureomycin gained a noticeable amount of weight in the 1940s, livestock farms have used antibiotics as growth boosters. Sub therapeutic antibiotic therapy (STAT), which was administered to pigs and chickens from 1946 to 1950 as a result of the occurrence, significantly increased the weight gain of the animals (15–20%). Taking into account the impact of antibiotics on animal weight gain, the FDA approved the use of antibiotics in livestock farms in 1951 (Castanon, 2007; Teillant & Laxminarayan, 2015).

Different theories have been put forth regarding the mechanisms of antibiotic growth promoters (Huyghebaert et al., 2011; Thacker, 2013), which include the following: (1) decreasing the frequency and severity of bacterial infections; (2) delaying the uptake of nutrients by microorganisms; (3) reducing the amount of growth-depressing metabolites secreted by gram-positive bacteria; and (4) improving nutrient absorption by thinned intestinal walls. Between 100,000 and 200,000 tons of antibiotics are overused and misused in animal farming worldwide now. Antibiotics utilized in animals raised for food can be divided into six main categories [22] (see Figure 1).

The most commonly used class of antibiotics on animal farms is discovered to be the sulphonamides, which are followed by fluoroquinolones, aminoglycosides ≈ phenicols ≈ β-lactams, and tetracyclines ≈ oxazolidinones. Antibiotics are often given to livestock through injection, drinking water, and feed in order to treat illnesses and encourage growth (Brown et al., 2017; Mungroo & Neethirajan, 2014).

Sulphonamides are the most frequently used antibiotics on livestock farms, followed by tetracyclines, aminoglycosides, phenicols, and fluoroquinolones. These antibiotics are given by injections, feed, and drinking water to treat diseases and promote growth (Clark et al., 2012). In North American chicken farming, antibiotics such as salinomycin, tetracycline, bacitracin, tylosin, virginiamycin, and bambermycin are often used. Tetracyclines account for an estimated 37% of antibiotics used for food-producing animals in the European Union (EU), compared to two-thirds in the United States (Carvalho & Santos, 2016).

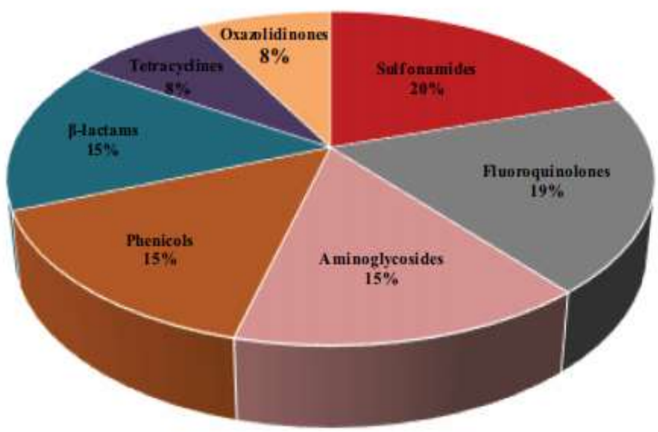

Figure 1 Classification of antibiotics used in food-producing animals (adapted) (Mungroo & Neethirajan, 2014).

In Germany, the most widely used antibiotic families were aminoglycosides (25.6%) and lincosamides (25.6%), followed by polypeptides (21.4%) and beta-lactams (16.2%) in research conducted on broiler chicken flocks. Overall, lincosamide and aminoglycoside consumption increased significantly over the six years of study. The proportion of treatments with polypeptides, macrolides, and fluoroquinolones declined in the following years compared to the first year of data collection (Kasabova et al., 2021).

A total of 350 feces samples were collected from a study that involved 40 pig farms from France and Italy and 35 broiler farms from Cyprus, Greece, and the Netherlands. Tetracyclines, penicillins, and sulfonamides were the most often sold antibiotic classes for animals raised for food, making up 32%, 26%, and 12% of all veterinary antibiotic sales, respectively, according to the research. The primary cause of this high antibiotic consumption is the widespread oral treatment of pigs, poultry, and cattle at the species level (Torren Edo, 2019; Van Boeckel et al., 2015).

According to a survey conducted on the usage of antibiotics in several poultry farms in Thailand, 14,000 3 kg hens were raised in 41 days using an antibiotic regimen that includes amoxicillin, colistin, doxycycline, oxytetracycline, and tilmicosin (Redwan Haque et al., 2023).

The first 1-4 days after delivery observed the usage of 4245 g of antibiotics (303 mg/chicken), which was then followed by 9-12 days, 15-18 days, 21-24 days, and 28-31 days, in that order.

Weak restrictions on veterinary medications in India have led to the overuse of antibiotics in animal farms, particularly the same antibiotics used for human therapy (Sharma et al., 2020).

Since 1989, China has increased the number of antibiotics used for cattle, with amoxicillin, florfenicol, lincomycin, penicillin, and enrofloxacin being used widely (Zhang et al., 2015).

Even though there are many regulations regarding the use of antibiotics, most countries in the world have widespread overuse and misuse of livestock farms (Hu & Cheng, 2016a), and developing nations use significantly more antibiotics on average than wealthy nations. However, the top five nations using excess veterinary medication on animal farms are China, the USA, Brazil, India, and Germany. It is estimated that by 2030, China alone will account for 30% of the world's veterinary antibiotic supply, up from 23% in 2010 (Van Boeckela et al., 2015). Minimal expense and inadequate oversight (Hu & Cheng, 2016b).

3. Guidelines for judicious use of veterinary antibiotics

This section should contain detailed information about the procedures and steps followed. It can be divided into subsections if several methods are described.

With the common objective of reducing antibiotic resistance, numerous guidelines are established by organizations concerning the use of veterinary antibiotics. The following is a summary of the main recommendations for the use of veterinary antibiotics: Antibiotics should only be prescribed to treat diseases with a bacterial aetiology; the administration of antibiotics to treat animals should be under the supervision of a veterinarian; and the health status of an infected animal should be prioritized before using antibiotics. Antibiotics may be recommended after an animal's preliminary diagnosis (Haag, 2014).

A maximum residual limit (MRL) for antibiotics that are allowed in animals reared for food has been established by the European Union (EU) (Redwan Haque et al., 2023). The maximum residue levels of veterinary antibiotics in different food specimens that the EU permits are shown in (Figure 2). The Food and Agriculture Organization/World Health Organization (FAO/WHO) has released guidelines on MRLs for veterinary antibiotics in animals used for food production. These guidelines have been approved by the US, the EU, and seventy other countries (Novaes et al., 2017).

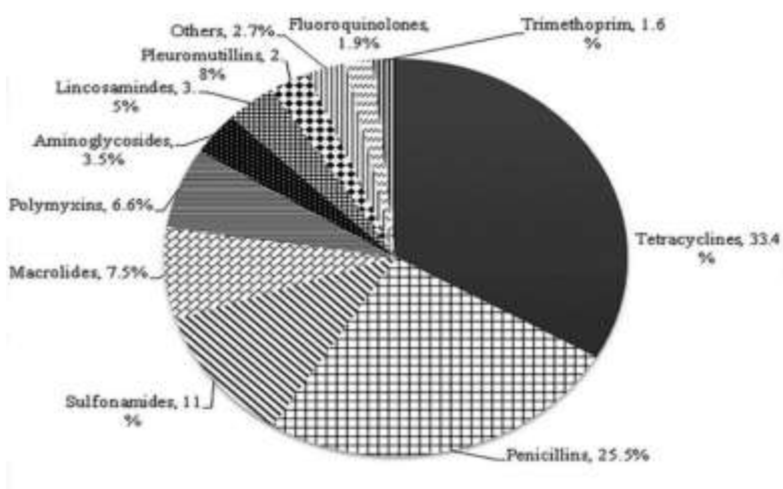

Figure 2 Veterinary antibiotics and their maximum residue levels in different food

However, Canada has its own regulation on MRLs, But in contrast to the FAO/WHO established limitations, Canada has its own regulation on MRLs for veterinary medications in foods derived from animal sources (Canada, 2017), which is stricter compared to the established limits by FAO/WHO. It is found that the MRL of an antibiotic largely depends on animal species and the target tissue. In addition to MRL, several other considerations for the consumption of foods from animal sources are taken into account to ensure food safety and minimize human health risks. For instance, MRLs of ampicillin in muscle, fat, liver, kidney, and milk from all possible sources are 50, 50, 50, 50, and 4 μg/kg, respectively, However, eating an egg that contains ampicillins is strictly forbidden for people. Similarly, when apramycin residue is detected in a cow's muscle, fat, liver, or kidney, humans cannot consume milk. The fact that developed country authorities have appropriate recommendations for food sample MRL and antibiotic use is important. One of the main causes of AR in foods derived from animals in emerging and poor countries may be the lack of specific guidance for farmers on the careful application of antibiotics (Ayukekbong et al., 2017).

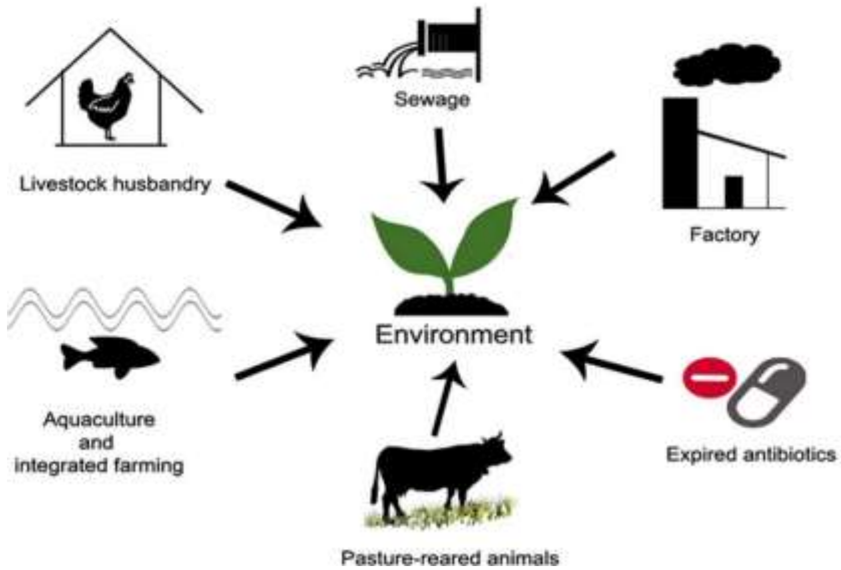

Figure 3 Multiple entry pathways of antibiotics into the environment.

Table 1. Excretion rate of selected antibiotics in animal (Kümmerer & Henninger, 2003).

Antibiotics	Excretion rate in animals
Tetracycline	75–80%
Lincosomides	60%
Macrolides	50–90%
Sulfamethazine	90%
Chlortetracycline	65%
Tylosin	50–100%
Norfloxacin	30%
Ofloxacin	90%
Sulfonamide	90%
Sulphamethoxazole	85%
Amoxicillin	10–20%
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Table 2. Approved antibiotics for food producing animals that are critically and highly important to human medicine (Redwan Haque et al., 2023).

Antibiotics	Importance to human medicine	Animal used
Aminoglycosides	Critically important	Swine, poultry
Lincosamides	Highly important	Swine, poultry
Macrolides	Critically important	Cattle, swine, poultry
Penicillins	Critically important	NA
Streptogramins	Highly important	Cattle, swine, poultry
Sulfonamides	Highly important	Cattle, swine, poultry
Tetracyclines	Highly important	Cattle, swine, poultry
Aminoglycosides	Critically important	Swine, poultry

4. Antibiotic residues in meat

This section is a comparative or descriptive analysis of the study based on the study results, previous literature, etc. The results should be offered in a logical sequence, giving the most important findings first and addressing the stated objectives. The author should deal only with new or important aspects of the results obtained. The relevance of the findings in the context of existing literature or contemporary practice should be addressed.

Meat is regarded as an effective source of zinc, vitamin B12, and protein. It is also thought to be an excellent source of the nine essential amino acids that our bodies require for healthy development and functioning (Ponnampalam et al., 2016).

Unfortunately, antimicrobial residues in these tissues can lead to a wide range of health problems, even with all of these advantages. It is true that the usage of antibiotics, such as oxytetracycline and Penicillin G, is necessary for treating some infections in animals as well as promoting better growth. An estimated 45 mg of antibiotics are used annually per kilogram of cattle worldwide (Ma et al., 2021).

Therefore, the probability of carcinogenicity, mutagenicity, and toxicity in human bodies exists if residues are found in any of its parts (Jaafar et al., 2021; Naous et al., 2018). The use of antibiotics to treat illnesses in animal husbandry has a significant impact on the distribution of antibiotics in meat from cattle and poultry. The antibiotic methenamine, which is prohibited in the USA, Russia, Australia, and New Zealand, is used to treat urinary tract infections and prevent bladder infections. This antibiotic works by producing formaldehyde in an acidic environment, and formaldehyde has antibacterial properties.

These days, there is growing worry over methenamine residue in beef due to possible negative health impacts. High performance liquid chromatography combined with tandem mass spectrometry (HPLC-MS/MS) was used to analyze the methenamine content of swine edible tissues, specifically the muscle, kidney, and liver that were taken from a Chinese local market (Xu et al., 2016). While methenamine levels in two kidney samples were determined to be 18.20 µg/kg and 41.70 µg/kg, methenamine was not present in muscle or liver. The use of HPLC-MS/MS to measure the amount of methenamine in edible tissues was also validated by this investigation. Furthermore, out of 35 fresh samples in Shanghai, the AR was found in 35.30% of the pork and 22.20% of the chicken. Tetracyclines and fluoroquinolones were the most common antibiotics found in meat samples. Norfloxacin residue levels were 27 ng/g in pork and 49.60 ng/g in chicken, with oxytetracycline (16.90 ng/g) in chicken coming in second (Wang et al., 2017).

In South Africa, 150 fresh meat samples of chicken, beef, and pig were analysed to look for four ARs using three different analytical techniques: ELISA, TLC, and HPLC (Ramatla et al., 2017). Every technique demonstrated the various fractions of ARs in the samples. The ELISA method revealed the concentrations of sulphanilamide, tetracycline, streptomycin, and ciprofloxacin to be 19.80-92.80 µg/kg, 26.6-489.10 µg/kg, 14.20-1280.80 µg/kg, and 42.60-355.60 µg/kg, respectively. The HPLC method demonstrated the concentrations to be 2 0.7-82.1 µg/kg, 41.8-320.8 µg/kg, 65.2-952.2 µg/kg, and 32.8-95.6 µg/kg.

However, the recommended limit for both streptomycin and ciprofloxacin MRLs, which is 100 µg/kg, was surpassed by the mean value of the residual levels (Alimentarius, 2011). The Premi test was applied for residual antibiotic study in pork in Madagascar (Rakotoharinome et al., 2014). In Madagascar, the Premi test was used to examine the persistence of antibiotics in pigs [50]. Among 360 samples, the incidence rates of AR were 34.42% in urban abattoirs and 42.20% in regional abattoirs. Drug residue in meat has been linked by authors to sick or undergoing treatment animals. In a similar vein, Shahbazi et al. (Shahbazi et al., 2015) found that out of 120 samples, including liver, thigh, and breast, 25% of poultry carcasses had tetracycline residue contamination.

Using ELISA and HPLC, the samples' mean tetracycline residue values ranged from 45–247.32 µg/kg to 31.40–889 µg/kg, respectively. In order to remove fluoroquinolones from meat samples, Timofeeva et al. (Timofeeva et al., 2020)] recently developed an inexpensive method based on deep eutectic solvent (DES) pretreatment. Findings demonstrated a very successful method for the separation of ofloxacin and fleroxacin in meat samples from chicken and beef, with extraction recovery rates ranging from 98% to 100%. To determine how long antibiotics would take to leave chicken tissue, a dose of minocycline (7 mg/kg) was given orally to the birds (Redwan Haque et al., 2023).

Minocycline was found to be widely distributed in various tissue samples. Up to the third day after the drug was taken orally, the amount discovered in all types of tissue samples ranged from 49.20 to 135.20 µg/kg. Additionally, kidneys continued to contain 11.80 µg/kg of minocycline until the seventh day following medication delivery. The risk factors of veterinary medication residue were examined by Beyene (Beyene, 2016), who concluded that if meat is kept out of the hands of animals for a longer period of time before they are killed for food, the residual effects of antibiotics would be low. It is crucial to remember that appropriate withdrawal times must be considered prior to marketing animals for safe human consumption.

5. Antibiotic residues in milk

The author should clearly explain the important conclusions of the research, highlighting its significance and relevance.

Dairy farms employ veterinary medications, primarily antibiotics, to treat and prevent a variety of illnesses. Common antibiotics that are used for their therapeutic and antimicrobial qualities against diseases, including mastitis, respiratory and digestive infections, include tetracycline, quinolone, lincomycin, streptomycin, and chloramphenicol (Niang et al., 2017). SNAP test kits were used in Palestine for quick screening during the first milk quality tests. Thirteen of the 34 samples, eight from different suppliers, had their beta lactam and tetracycline content examined. Three tetracyclines and four beta lactams tested positive in the results (Al Zuheir, 2012).

The existence of antibiotic residues (AR) in the milk of various animal species resulting from the excessive and improper administration of antibiotics is elaborated upon below: As individual milk consumption increased from 4.89 kg in 1997 to 36.20 kg in 2016 (Gao et al., 2017), pasteurized and ultra-high temperature milk are the most popular dairy products in China. However, it is concerning that 15 screened antibiotics, including human antibiotics with different fractions, have been found in dairy products in China. Only two human antibiotics, cefradine and chloramphenicol, were detected frequently (10.60% of the antibiotics listed above). A preliminary investigation found that milk taken from ten Chinese provinces contained sulphonamides (20.10%) and fluoroquinolones (47.20%) (Redwan Haque et al., 2023).

In UHT milk available in China, another study demonstrated a relatively higher detection rate of streptomycin (15.50%) than that of tetracycline (4.70%), quinolone (3.30%), and lincomycin (2.70%). The highest recorded concentrations of streptomycin, tetracycline, quinolone, and lincomycin in milk are 8.92 µg/kg, 9.06 µg/kg, 4.06 µg/kg, and 7.66 µg/kg, respectively (Du et al., 2019).

Antibiotics such as tetracycline, sulphonamide, and quinolone were found in some other studies (Cui, 2011) with maximal residue values of 47.70 µg/kg, 20.24 µg/kg, and 20.49 µg/kg, respectively. It should be mentioned that heating milk does not totally eliminate drug residues; as a result, processed milk and dairy products still contain AR (Roca et al., 2010; Roca et al., 2011).

Out of 100 pasteurized milk samples, three samples—oxytetracycline (121.80 µg/kg), tetracycline (93.50 µg/kg), chlortetracycline (61.60 µg/kg), and doxycycline (73 µg/kg)—were found to contain AR at different percentages in Brazil (Redwan Haque et al., 2023). Tetracycline is present in only 3% of Brazilian milk samples, with 2% of those samples having tetracycline residue that is higher than the MRL (100 µg/kg) (FOOD).

Abbasi (Abbasi et al., 2011) assessed the amount of tetracycline in 90 pasteurized, 10 sterilized, and 14 raw milk samples from Iran in a study. While pasteurized and sterilized milk had comparatively lower levels of tetracycline—87.10 ng/g and 112 ng/g, respectively—than raw milk (154 ng/g), the mean total tetracycline residues for all samples was 97.60 ng/g. Tetracycline detection in milk was found in greater quantities in Croatia (76%) compared to Brazil (14%) and China (2.80%), according to a comparative examination of AR in milk samples from many different countries.

China exhibited the highest residue level at 47.70 µg/kg, with Brazil following closely behind at 11.40 µg/kg and Croatia at 4.26 µg/kg. Although the overall residue level (5047.30 µg/kg) found in milk samples from Mexico was 200 times greater than that found in China (4.06 µg/kg), the identified rates of quinolone in China and Mexico were equal. As a result, it should be mentioned that ARs are found in milk and dairy products everywhere, which is causing increasing concern for everyone due to the possibility of antibiotic resistance in humans.

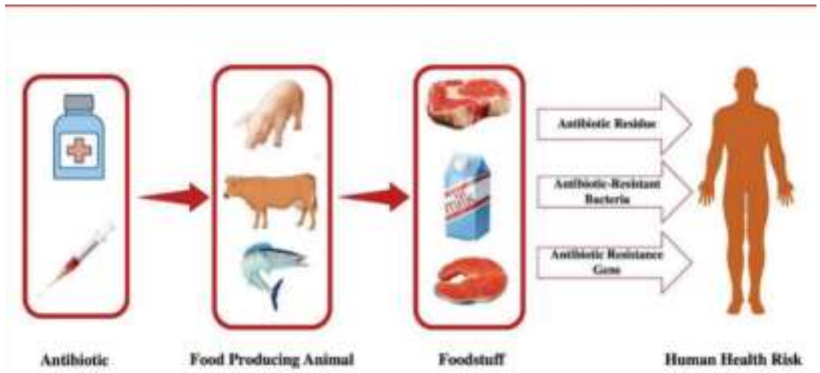

Figure 3. Human health concerns of ARs in foodstuffs from animal sources.

A 5-day withdrawal period following the extralabel use of gentamicin in nursing cows for mastitis may not be sufficient to ensure the safety of milk products, according to a study on gentamicin residues in milk. Even though just one cow out of 34 had medication residues visible for more than five days, our findings suggest that a five-day withdrawal period might not be enough to stop this antibiotic from contaminating milk (Tan et al., 2007).

6. Conclusion

Antibiotics are used on animal farms to treat illnesses of animals that suffer from bacterial infections. However, overdosing results in the accumulation of antibiotics in the organs and bodily tissues of animals reared for food, which has become an increasingly serious global health concern for people. It has been reported that while certain processing techniques, such as heat treatment, can lower the amount of AR in food samples, they cannot entirely eliminate it.

However, there are a number of bacteria that are resistant to antibiotics, including Salmonella species, Campylobacter species, Staphylococcus species, and enterotoxigenic E. coli, which are frequently found in the bodies of animals. For example, Salmonella enterica isolated from chicken and egg carcasses is resistant to tetracycline, quinolone, streptomycin, penicillin, and sulphisoxazole, which ultimately infect humans and cause gastrointestinal disorders. Antibiotic-resistant genes in humans may have originated from the consumption of antibiotics given to animals. Since organic farming may have a lower rate of antibiotic-resistant genes, the current study recommends using bioactive ingredients such as probiotics, organic acids, amino acids, and enzymes as an alternative to antibiotics in animal farms.

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ORCID Id: (0009-0002-5864-1882)

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