

Transmission of Antibiotic Resistance Genes through Animal-Origin Food: A Narrative Review

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Review Article

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Received in 3/11/2024

Accepted in 1/12/2024

Abstract

Antibiotics are necessary for human and animal health because they resist and overcome bacterial infections and save life. However, the wide spread and often inappropriate antibiotic usage has resulted in the emergence of antimicrobial resistance (AMR), suggesting serious risks to worldwide healthcare systems. This narrative review digs into the transmission of antibiotic resistance genes via animal-origin food, offering light on the methods by which antibiotic resistance spreads and the implications for public health. It emphasizes the crucial necessity for prudent antibiotic prescribing practices, surveillance system enhancement, and the investigation of alternate techniques to minimize antibiotic resistance and ensure antibiotic efficacy. Through an investigation of the many resistance mechanisms deployed by bacteria, both intrinsic and acquired, this article emphasizes, the need for novel techniques to prevent biofilm formation on food contact surfaces and prevent the spread of antibiotic resistance within the food sector.

Keywords: *Antibiotic resistance, Electrolyzed water, Food of animal origin, Innovative techniques*

Introduction

Antibiotics safeguard human and animal health by struggling bacterial infections and preserving life. They are critical in the fields of healthcare, veterinary medicine, and agriculture. Antibiotics simplicity of access and low cost led to enhanced human health and life expectancy, and they became one of current medicine primary techniques. They are the most widely prescribed medicines currently, although nearly half of them are inappropriate. As a result, antimicrobial resistance (AMR) developed and became an increasingly serious

threat which hinder to combat bacterial infections. However, improper application and excessive dependence on antibiotics have led in a development of antibiotic resistance, which defines an overwhelming global health concern **Samtiya et al. (2022)**.

In order to tackle this issue, it is essential to adhere to the prescription guidelines **Muteeb et al. (2023)**. In the 1940s, it was demonstrated that feeding sub-therapeutic doses of antibiotics improved feed competence and accelerated growth of animal, which was followed by a large-scale usage of antibiotics in food animal

production. In animals, antibiotics have been used at prophylactic levels for diseases preventing and at metaphylaxis levels to treat diseased animals, that preventing disease spread. The widespread, long-term use of antibiotics and potentially their misuse led to the development of antimicrobial-resistant bacteria, creating a major health hazard to humans and animals **Vinayamohan *et al.* (2022)**. The expansion of antibiotic-resistant bacteria (ARB) has become a major risk facing the world, especially in foods of animal origin **Blanco-Picazo *et al.* (2022)**, leading to drugs ineffectiveness so that increased number of deaths **Jampani *et al.* (2022)**. WHO evaluated the extent of antimicrobial resistance globally, results were dramatic, showing that many areas of the globe (e.g., Eastern Mediterranean, South-East Asia Region, among others) showed resistance levels by common bacteria that had reached troubling levels. The threat and costs of AMR are widely known. Antibiotic-resistant contaminations, for instance, cause about 33,000 deaths in Europe and 4.95 million deaths worldwide per year, cost about 1.5 billion EUR in healthcare plus productivity losing. The World Health Organization considers AMR "one of the ten global public health alerts facing humanity" based on estimates that, by 2050, it will be accountable for more than 10 million deaths per year, a worldwide economic cost of more than 100 trillion dollars **Caneschi *et al.* (2023)**.

Bacteria can transmit through animal-based food through various technique, as well as processing, cross-contamination, inadequate cooking, improper storage, and consumption of raw or undercooked products. The familiar food-borne pathogens from animal products, like *E. coli*, *Salmonella*, *Campylobacter*, *Listeria monocytogenes*, and *Staphylococcus aureus*, can cause food-borne disorder in humans **Urban-Chmiel *et al.* (2022)**.

A concerted effort involving healthcare professionals, veterinarians, policymakers, and the agricultural industry is necessary to uphold the effectiveness of antibiotics. Promoting responsible antibiotic usage, strengthening surveillance systems, and exploring alternative strategies can help alleviate antibiotic resistance and guarantee the sustained efficacy of antibiotics

Muteeb *et al.* (2023).

The scope of this narrative review highlighted its significance to comprehending the dissemination of antibiotic resistance genes (ARGs) through animal-derived foods and the possibility of hazards to the general population. Discussing the various resistance mechanisms used by bacteria, both intrinsic and acquired, and how they contribute to antibiotic resistance. The paper looks at how food-borne bacteria develop biofilms on food contact surfaces, and its reflection on food safety and quality. The review also underlines the importance of safe and creative approaches to properly managing biofilms on contact surfaces and preventing antibiotic resistance in the food business.

Potential sources of Antibiotic resistance genes in animal environment

Animal environment, such as water, soil, and equipment are important sources of antibiotic- and antibiotic-resistant bacteria (ARB) that the animal acquires and subsequently present in its products that tend to transmit to consumers through the food chain.

Water is an essential source of antibiotic and ARB transport; studies have shown that water bodies contain high concentrations of antibiotics. Which subsequently increases the chances of emergence of ARB and thus the spread of antibiotic-resistant genes **Jampani *et al.* (2022)**. These water bodies are then used as a source for animal drinking or irrigation of the crops on which the animal feeds and thus the presence of this ARB and antibiotic-resistant genes (ARGs) in the animal's products **Liu *et al.* (2022)**.

Soil of animal-feed crops also plays an important role as a source of antibiotic-resistant bacteria. It appears that antibiotics are used during animal and livestock husbandry, and then these antibiotics are released with animal stool and urine, recycled and used as natural fertilizer for soil, causing soil contamination and consequently the development of ARB and naturally increasing the probability of biological crops contamination **Ishikawa *et al.* (2018)**. A study from Bangladesh reported the presence of antibiotic-resistant *salmonella* when they took a swab from poultry litter

(used as a fertilizer) and anus, indicating that the soil could be contaminated with ARB **Alam et al. (2020)**. Another study from China established ten of antibiotic-resistant genes, two of genetic mobile elements were present in fertilizer samples of chicks, cows and swine **Wang et al. (2019)**.

Animal to animal transmission was suggested by a study from Iran, authors found that dairy products had a simple resistance to chloramphenicol that resulted from resistance gene transmission to livestock due to its presence beside a poultry farm **Moghimi et al. (2023)**.

Antibiotics are used for prophylaxis in the treatment of entire livestock, including animals that exhibit no clinical signs of infection, to prevent the transmission of disease. Besides the overuse of broad-spectrum antimicrobials in animals and the usage of not approved or are unauthorized medications **De Mesquita Souza Saraiva et al. (2021)**.

Antibiotics are also utilized as growth promoters, which are antimicrobials added to animal feed at low doses to improve animal performance, raising the possibility that trace amounts of antibiotics could contaminate food and feed **Samtiya et al. (2022)**. The drug's use might leave antibiotic residues in foods like meat, eggs, and milk. As a result, food-borne microbes develop resistance and can pass on their resistance genes to both clonal descendants and other isolates from the same bacterial species or even different species **De Mesquita Souza Saraiva et al. (2021)**. A study in 2015 discovered the potential contamination of *Campylobacter jejuni* in the place of poultry slaughter **Manson et al. (2019)**. Another study in Egypt, based on the collection of 178 samples including meat, fish and milk products, found that among the causes of sample contamination are various stages of manufacturing, including storage and transportation **Khater et al. (2021)**. The processing phase is most prone to the occurrence of antibiotic-resistant bacteria, mixing meat of high-quality farm with low-quality meat may occur during the processing thus cross contamination with ARB and ARGs could be occurred. In a study conducted in the United States, authors concluded that the most important step is the

cleanliness of the vessels used in the processing **Manson et al. (2019)**. Even the air in the factory environment may represent a source of transmission antibiotic resistance **Blanco-Picazo et al. (2022)**. Non-digested antibiotics leakage into the environment could be a disaster especially when released in animal products as mentioned in many studies. Antimicrobial residues have been identified in chicken flesh pieces sold in Egypt, cooking can diminish antibiotic residues, at least partially **Kamouh et al. (2024)**. It has been found that heat treatment in different time-temperature combinations destroys or even lowers antibiotic medication residues in animal products. However, cooking procedures do not ensure complete breakdown of antimicrobial medication residues **Pame et al. (2024)**.

The prevalence of antibiotic-resistant bacteria in various animal species and geographical regions.

Determination the extent to which AMR spreads through the food chain is so difficult. Animal food products are the major source of AMR bacteria. Over time, Food-borne illnesses have become the leading cause of morbidity and death globally. Many food stakeholders are concerned about antimicrobial resistance (AMR), which has the possibility to influence human health on a global scale **Samtiya et al. (2022)**.

Animals share many infectious diseases with humans (e.g., bacterial, viral, parasitic), though they are usually caused by different etiological agents. Hence, it is also common to share medications, as well as antibiotics with difference in concentrations and purity. As highlight by Regulation (EU) 2019/6, the AMR phenomenon in animals is much more complex than it is in humans and requires an even more attentive and conscious use of antibiotics **Caneschi et al. (2023)**.

Table (1)

Organism	Common Strains\ Species\ Groups	Resistance Genes	Target Antibiotics	Source	Reference
<i>Escherichia coli</i>	Commensal <i>E. coli</i> . Pathogenic <i>E. coli</i> which classified into:	<i>bla</i> _{CTX-M} <i>genes as</i> (<i>bla</i> _{CTX-M-1} , <i>bla</i> _{CTX-M-2} , <i>bla</i> _{CTX-M-5} , <i>bla</i> _{CTX-M-9} , <i>bla</i> _{CTX-M-14} , <i>bla</i> _{CTX-M-15} , <i>bla</i> _{CTX-M-32} , <i>bla</i> _{CTX-M-55})	Tetracyclines β-lactams which contain penicillins as (Ampicillin), First, Second, Third, 4th Generations Cephalosporins as (Cefotaxime, Ceftriaxone, Cefepime), monobactams as (Aztreonam), carbapenems, and Cephamycin.	Beef, pork, meats from broilers, and turkey and their derivatives as sausages.	Ramos <i>et al.</i> (2020) Wakeham (2013) Gruel <i>et al.</i> (2021) De Alcântara Rodrigues <i>et al.</i> (2020)
	Intestinal pathogenic <i>E. coli</i> (IPEC):		(Cefotaxime, Ceftriaxone, Cefepime), monobactams as (Aztreonam), carbapenems, and Cephamycin.	Poultry, eggs, eggshells, and ovaries.	
	Enterotoxigenic <i>Escherichia coli</i> (ETEC)		Aminoglycosides as Neomycin and Streptomycin	Food Contaminated with Cattle and chickens	
	Enterohemorrhagic <i>E. coli</i> (EHEC) may also be referred to as Verocytotoxin-producing <i>E. coli</i> (VTEC) or Shiga toxin-producing <i>E. coli</i> (STEC) which includes <i>E. coli</i> O157:H7	<i>mcr-1 gene</i> <i>bla</i> _{TEM} <i>gene-sas</i> <i>bla</i> _{TEM-52} , <i>bla</i> _{TEM-1C} , <i>bla</i> _{TEM-1B}	Sulphonamides as Sulfamethoxazole, Trimethoprim-Sulfamethoxazole	Wastes.	
	Enteropathogenic <i>E. coli</i> (EPEC)	<i>bland</i> _{M-1} , <i>blasHV</i> ₁₂ , <i>bla</i> _{OXA} , and <i>bla</i> _{CMY} <i>genes</i>	Pirimidines as Trimethoprim	Cattle, dairy cattle farms, milk from cows with mastitis, raw milk and its derivatives such as cheese, pigs, fish, and turkeys.	
	Enterotoxigenic <i>E. coli</i> (EAEC)		Quinolones as Nalidixic acid		
	Enteroinvasive <i>E. coli</i> (EIEC)	<i>sul</i> <i>genes</i> <i>assul</i> <i>1, sul2, sul3</i>	Fluoroquinolones as Ciprofloxacin		
	Diffusely adherent <i>E. coli</i> (DAEC)		Macrolides		
	Extraintestinal pathogenic <i>E. coli</i> (ExPEC):	<i>tet</i> <i>genes</i> <i>astet</i> (A), <i>tet</i> (B) and <i>tet</i> (C)	Chloramphenicol		
	Uropathogenic <i>E. coli</i>		Fosfomycin		
	Sepsis-associated <i>E. coli</i>	<i>cfr gene</i>	Linezolid		
	Meningitis-associated <i>E. coli</i>	<i>ant</i> (3)-I	Polymyxins as Colistin		
	Ex:	<i>aac</i> (3)-I			
	<i>E. coli</i> O25:H4-B2-ST131 is an emerging resistant ExPEC lineage, other examples are ESBL-producing <i>E. coli</i> ST10, ST23, ST69, ST405 and O15:K52:H1.	<i>floR</i> <i>dfrA1</i> <i>str gene-sas</i> <i>strA</i> <i>qnrS1 genes</i>			

Table (1). (Continued)

<p>Salmonella spp.</p>	<p>There are two known species, which are:</p> <p><i>Salmonella bongori</i></p> <p><i>Salmonella enterica</i>, it is further divided into six subspecies:</p> <p><i>Salmonella enterica subsp enterica I.</i></p> <p><i>Salmonella enterica subsp salamae II.</i></p> <p><i>Salmonella enterica subsp arizonae IIIa.</i></p> <p><i>Salmonella enterica subsp diarizonae IIIb.</i></p> <p><i>Salmonella enterica subsp housemate IV.</i></p> <p><i>Salmonella enterica subsp indica VI.</i></p> <p><i>Salmonella enterica subsp enterica I</i> contain over 2,300 serovars. Serotypes can be categorized as:</p> <p>Typhoidal serotype, ex:</p> <p><i>Salmonella enterica serotypes Typhi</i></p> <p><i>Salmonella enterica serotypes Paratyphi</i></p> <p>Nontyphoidal serotypes, ex:</p> <p><i>Salmonella enterica serotype Enteritidis</i></p> <p><i>Salmonella enterica serotype Typhimurium</i></p> <p>Examples of <i>Salmonella</i> isolated from food of animal origin:</p> <p><i>S. Enteritidis</i></p> <p><i>S. Infantis</i></p> <p><i>S. Schwarzengrund</i></p> <p><i>S. Livingstone</i></p> <p><i>S. Vuadens</i></p> <p><i>S. Hadar</i> and other untypable isolates.</p>	<p><i>bla_{CTXM-15}</i>, <i>bla_{CTX-M-15}</i>, <i>bla_{CTX-M-14}</i> and <i>bla_{TEM}</i></p> <p><i>mcr-1 gene</i></p> <p><i>qnrB</i></p> <p><i>aphA1</i></p> <p><i>aadA</i>, <i>aadA2</i></p> <p><i>aac(3)IV</i></p> <p><i>sul genes</i> <i>assul1</i></p> <p><i>tet gene-sa</i> <i>tet(A)</i> and <i>tet(B)</i></p> <p><i>dfx12</i></p>	<p>B-Lactams Which Contain Penicillins as (Ticarcillin, Amoxicillin, Ampicillin), Cephalosporins as (Cefepime, Ceftazidime, Cefoxitin, Ceftriaxone, Cefotaxime and Cefuroxime) and Monobactams as (Aztreonam).</p> <p>Quinolones as Norfloxacin and Nalidixic Acid</p> <p>Pyrimidines as Trimethoprim</p> <p>Chloramphenicol</p> <p>Aminoglycosides as Streptomycin and Gentamicin</p> <p>Sulfonamides as Sulfisoxazole, Sulfafurazole and Trimethoprim-Sulfamethoxazole</p> <p>Tetracyclines</p> <p>Polymyxins as Polymyxin and Colistin</p> <p>Fluoroquinolones as Ciprofloxacin</p>	<p>Pigs, cattle, fish, shrimp, poultry, turkey, and eggs.</p> <p>Duck and poultry meat and bone, beef, minced pork, and meat products such as sausages and shawarma.</p> <p>Semi-finished meat products, ready-to-cook meat, and ready-made fish dishes.</p> <p>Milk and milk products as cheese.</p> <p>Consumption of food contaminated with feces.</p>	<p>Kozytska et al. (2023)</p> <p>De Alcântara Rodrigues et al. (2020)</p> <p>Porwollik et al. (2004)</p>
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Table (1). (Continued)

Campylobacter spp.	<p>It contains 32 species, and 9 subspecies, such as:</p> <p><i>Campylobacter jejuni</i> (<i>C. jejuni</i>)</p> <p><i>Campylobacter coli</i> (<i>C. coli</i>)</p> <p><i>Campylobacter upsaliensis</i> (<i>C. Upsaliensis</i>)</p> <p><i>Campylobacter lariidis</i> (<i>C. Lari</i>)</p>	<p><i>cfr(C) gene</i></p> <p><i>erm(B) gene</i></p> <p><i>tet gene-sastet(L) and, tet(O) gene, tet(M) gene</i></p> <p><i>mutation in gyrA and gyrB genes</i></p> <p><i>mutation in the 23S rRNA gene</i></p> <p><i>cmeB genes</i></p> <p><i>bla_{OXA-61} gene</i></p> <p><i>aacA4</i></p> <p><i>aacA/aphD</i></p> <p><i>aph(2'')-If</i></p> <p><i>aph(2'')-Ig</i></p>	<p>B-Lactams Which Contain Penicillins as (Amoxicillin, Ampicillin, Amoxicillin-Clavulanic acid), Cephalosporins as (Ceftiofur, Cephalothin, Ceftriaxone) and Monobactams as (Aztreonam), Carbapenems as (Meropenem).</p> <p>Linezolid</p> <p>Macrolides as Clarithromycin, Erythromycin, Azithromycin and Tylosin</p> <p>Tetracyclines as Oxytetracycline and Doxycycline</p> <p>Amphenicols as Florfenicol and Chloramphenicol</p> <p>Fluoroquinolones as Ciprofloxacin and Enrofloxacin</p> <p>Aminoglycosides as Neomycin, Streptomycin, Kanamycin and Gentamicin</p> <p>Quinolones as Nalidixic Acid and Norfloxacin</p> <p>Lincosamides as Lincomycin and Clindamycin</p> <p>Spectinomycin</p> <p>Polymyxins as Colistin</p> <p>Pyrimidines as Trimethoprim</p> <p>Sulfonamides as Sulfamethoxazole/Trimethoprim.</p> <p>Telithromycin</p>	<p>Product contaminated with feces of pig and laying hens.</p> <p>Pork, beef, poultry meat, chilled chicken, and milk and derived dairy products.</p> <p>Pig, sheep, cattle and poultry, slaughterhouses, chicken products, equipments in processing plants.</p> <p>Chicken and turkey carcasses.</p>	<p>De Alcântara Rodrigues <i>et al.</i> (2020)</p> <p>Melo <i>et al.</i> (2019)</p> <p>Portes <i>et al.</i> (2023)</p>
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Table (1). (Continued)

<i>Staphylococcus aureus</i>	Enterotoxigenic <i>Staphylococcus aureus</i> non-enterotoxigenic <i>Staphylococcus aureus</i>	<i>tet</i> gene- <i>sastet(K)</i> and <i>tet(M)</i> gene <i>mecA</i> gene <i>erm</i> gene- <i>saserm(A)</i> and <i>erm</i> (<i>B</i>) <i>cfr</i> gene <i>gyrA</i> and <i>gyrB</i> <i>aadD</i> gene <i>aadE</i> gene <i>str</i> genes <i>bla_{ARL}</i> and <i>blaZ</i> genes <i>msr</i> re- sistance genes <i>asmsrA</i> and <i>msrB</i> .	B-Lactams Which Con- tain Penicillins as (Methicillin and Ampicillin), and Cephalosporins. Macrolides as Erythromycin Fluoroquinolones as Ciprofloxacin Lincosamides Aminoglycosides as Streptomycin Phenicol Oxazolidinones Pleuromutilins Vancomycin Tetracyclines Sulfonamides as Sulfamethoxazole Pyrimidines as Trimethoprim Streptogamines as Streptogamine B	Beef, fish, shrimp, chicken and poultry products as eggs and eggshell. Chicken feces and different meat samples. Milk samples and dairy products (cheeses and yogurt).	De Alcântara Rodrigues <i>et al.</i> (2020)
Enterococci spp.	<i>Enterococcus faecium</i> <i>Enterococcus faecalis</i> <i>Enterococcus gallinarum</i>	<i>optrA</i> gene <i>van</i> gene- <i>sasvanA</i> , <i>vanB</i> , and <i>vanC-1</i> <i>mrs</i> genes as <i>mrsA</i> and <i>mrsB</i> <i>linA</i> gene <i>erm</i> gene- <i>sasermA</i> , <i>ermB</i> , and <i>ermC</i> <i>tet</i> genes as <i>tetK</i> , <i>tetL</i> , <i>tetM</i> , <i>tetO</i> , and <i>tetS</i>	Macrolides as Erythromycin Tetracyclines Oxytetracycline Lincosamides Vancomycin B-Lactams Which Contain Penicillins (Ampicillin), Rimfamycin Aminoglycosides as Streptomycin, Kanamycin, Fluoroquinolones and Ciprofloxacin	laying hens, cattle, swine fecal samples. cheeses, raw milk integrated fish and poultry farm, Beef, and chicken meat.	
Klebsiella spp.	<i>Klebsiella pneumoniae</i>	<i>bla_{SHV}</i> , <i>bla_{CTX-M-1}</i> and <i>bla_{CTX-M-10}</i>	β -lactam resistance	Chicken meat	
Yersinia spp.	<i>Yersinia enterocolitica</i>	-----	β -lactams which contain penicillins as (Ampicillin, amoxicillin, and Ticarcillin), Cephalosporins as (cefotaxime). tetracyclines Fluoroquinolones as Ciprofloxacin	Meat, birds, chicken, Pigs, raw milk and milk products.	

Mechanisms by which bacteria acquire antibiotic resistance genes.

Certain bacteria show resistance to antibiotics due to structural or functional features **Kardomatea (2022)**. Numerous microbes use a variety of resistance mechanisms, some of which are "intrinsic or inherent," meaning that the cell can use genes which already possesses to survive **Darby *et al.* (2022)**. These mechanisms occurred prior to the discovery of antimicrobial agents **Aworh *et al.* (2021)**.

Other mechanisms are "acquired," where the organisms gaining of new genetic material leads to the development of new capacities that mediate survival **Darby *et al.* (2022)**. Even at sublethal concentrations, antimicrobial compounds influence bacterial physiology and adaptive microbial evolution, as well as perhaps act as signaling molecules that control the expression of microbial and host genes **Samtiya *et al.* (2022)**.

Bacteria might be intrinsically resistant to antibiotics due to functional and structural properties, or they can acquire resistance to antimicrobial drugs through:

Vertical Gene Transfer (VGT) through *de novo* mutations: When spontaneous mutations occur in pre-existing or newly acquired genes in their chromosomal DNA, which are then passed to progeny **Samtiya *et al.* (2022)**.

Horizontal Gene Transfer (HGT): It occurs by acquiring antimicrobial resistance genes (ARGs) through cell-to-cell genetic material transmission, either from close relatives or even other species, which then pass to their progeny **De Mesquita Souza Saraiva *et al.* (2021)**.

The three major mechanisms by which bacteria transfer genes horizontally are:

- **Conjugation:** It occurs by using Mobile genetic elements (mges) which are sections of genetic material that may transfer between or within genomes and include plasmids, insertion sequences (IS), transposons, and bacteriophages **Carr *et al.* (2021)**. Conjugative plasmids and transposons are the most common vectors for the transfer of antimicrobial resistance genes **De Mesquita Souza Saraiva *et al.* (2022)**. Plasmids are extra-chromosomal DNA molecules with sizes ranging from 2 to >100 kb

that replicate autonomously. Plasmids are exchanged between cells via the mating-pore pilus when they come into physical contact **Samtiya *et al.* (2022)**. Antibiotic resistance in Gram-negative bacteria has been mostly associated with DNA exchange via conjugation of plasmids containing ARGs **De Mesquita Souza Saraiva *et al.* (2022)**.

- **Transduction:** Bacterial transduction is the process by which DNA is transferred from one bacterium to another via bacteriophages **De Mesquita Souza Saraiva *et al.* (2022)**. Bacteriophages may occasionally integrate bacterial DNA instead of phage DNA in their capsid after lysing the bacterial cell and injects this DNA into another bacterial cell. Transduction may be separated into two types: general and specialized. Phages may contain and transmit any segment of the bacterial chromosome or MGEs in generalized transduction, but only the DNA proximal to the first integrated prophages can be contained and transmitted in specialized transduction **Liu *et al.* (2022)**.
- **Transformation:** Assimilation of exogenous free naked DNA, either single or double-stranded, into the cell after it has been released by dead and lysed cells carrying resistance genes **Samtiya *et al.* (2022)**. Following that, this DNA recombines with the chromosome of the receiving cell, including extra genes from the incoming DNA **Nadeem *et al.* (2020)**.
- **Vertical Gene Transfer (VGT) and Horizontal Gene Transfer (HGT) can occur at the same time** **Samtiya *et al.* (2022)** as a result, antibiotic resistance can spread and render previously effective antibiotics useless **Kardomatea (2022)**.
- **Overview of the bacterial defense mechanisms regarding antibiotics:** Bacterial strains must be capable to interfere with one or more of the critical phases required for the antibacterial agent's efficient action to allow them remain alive in the presence of an antibiotic.
- Bacterial species utilize one of four vital survival strategies **Chinemerem Nwobodo *et al.* (2022)**.

1. By lowering the permeability of the bacterial cell's membrane, the drug can't reach the target it was designed to reach **Darby et al. (2022)**.
2. Antibacterial drugs get removed from cells through the efflux pump mechanism. Trans-membrane efflux pumps, which transfer antibiotics from bacterial cells and decrease their intracellular concentration, enhance active efflux **Darby et al. (2022)**.
3. Enzymes deteriorate or modify antibiotic molecules, making them inactive. Enzymatic degradation involves the hydrolysis of the antibiotic's functional group, rendering it useless. Antibiotic modifying enzymes add different chemical groups to the antibiotic, preventing it from attaching to its target **Darby et al. (2022)**.
4. Changes in the antibacterial target within the bacterium lead the antibiotic to fail to bind and harm the bacterial cell. This can include changes in the gene that encodes the antibiotic's protein target or an enzymatic change of the binding site by a new protein that is not inhibited by the antibiotic **Schaenzer and Wright (2020)**. Target protection, in general, comprises the physical contact of a target protection protein with an antibiotic target, releasing it from antibiotic-mediated inhibition **Wilson et al. (2020)**.

which acquire antibiotic resistance genes and transmit through food chain **Manson et al. (2019)**.

Some fish farms have also used antibiotics to improve fish growth which has led to an increase in ARB **Tenover and McGowan (2008)**. A study in the United States, revealed that using *E. faecium* as a probiotic in chicken husbandry led to transmission of antibiotic-resistant genes through chicken meat **Manson et al. (2019)**.

Transfer of Antibiotic-Resistant Genes through food chain

Animal feed is the most important source of ARB, most farmers use antibiotics in animal feed for two reasons either to treat the animal if it is sick or to protect the animal from getting sick **Jahantigh et al. (2020)**. If the animals are sick, it is important to wait for withdrawal period of the drug in the post-sickness recovery phase and discard any products from these animals during this period **Qamar et al. (2023)** to avoid excretion of antibiotic through food and disturbing human gut microbiota and acquiring resistance.

The use of antibiotics or some types of bacteria as dietary supplements as a growth promoters and protection from diseases is a crucial problem and another important source of bacteria

Table (2). Common Antibiotic Classes and their resistance genes

Antibiotic Classes	Resistance Mechanisms	Target re-sistance	References	Antibiotic-resistant genes (ARGs)	References
Aminoglycoside (Gentamycin, Streptomycin, Kanamycin, and Neomycin).	Enzyme modification, decreased permeability	(ribosome), and Efflux pumps	Wu-Wu, <i>et al.</i> (2023)	<i>aac, aad, aadA5</i> , etc	Xu, <i>et al.</i> (2022).
Beta-lactams (Amoxicillin, Ampicillin, Cephalexin, Cefotaxime, and Benzylpenicillin)	Reduced permeability, Altered penicillin-binding proteins (PBPs), β -Lactamases, cephalosporinases, and Efflux pumps			<i>blaCTX-M-1, blaCTX-M-8, blaCTX-M-14, blaCTX-M-15, blaOXA-48, blaOXA-58, blaCTX-M, blaCMY-2, blaD-WA1~4, blaDWB1, blaTEM, mecA, ampC</i> , etc	
Macrolides (Azithromycin, Clarithromycin, Erythromycin, Roxithromycin, and Tylosin)	Enzyme modification, Decreased permeability, and decreased ribosomal binding			23S rRNA (<i>rrn</i> operon), <i>erm(B)</i> , <i>rplD</i> , <i>rplV</i> , <i>cme-ABC</i> , <i>mph(A)</i> , <i>mph(B)</i> , <i>inu (F)</i> , etc	Kim & Ahn, (2022)
Sulfonamides (Sulfamethoxazole, and Trimethoprim)	Resistance Mechanisms are Decreased permeability, and Production of drug-insensitive enzymes		Wu-Wu, <i>et al.</i> (2023)	<i>sulI, sulII, sul3</i> , etc	
Tetracycline (Doxycycline, Oxytetracycline, and Tetracycline)	Target resistance (ribosome), Drug detoxification, and Efflux pumps			<i>tetA, tetB, tetC, tetG, tetO, tetM, tetX</i> and <i>tetW</i> , etc	Xu, <i>et al.</i> (2022)
Quinolones (Ciprofloxacin, Enrofloxacin, Flumequine, Norfloxacin, Levofloxacin, Nalidixic acid, and Ofloxacin)	DNA gyrase, topoisomerase IV), Efflux pumps, and Decreased permeability				
Chloramphenicols (Thiamphenicol, Florfenicol, and Chloramphenicol)	Enzyme modification, Decreased permeability, Decreased ribosomal binding, and Efflux pumps				
Lincosamides (Lincomycin)	Enzyme modification, Decreased permeability, and decreased ribosomal binding				

Biofilm formation in food industry

According to estimates, biofilms account for around 80% of bacterial illnesses, and biofilms are resistant up to 1,000 times higher than those planktonic cells **Giaouris et al. (2014)**. Whereas, it is challenging to completely inactivate and remove mature biofilms that have been generated by food-borne pathogens on processing equipment and contact surfaces; any viable pathogens in detached biofilms could therefore result in cross-contamination of food items. Meanwhile, biofilm formation in processing environments is affecting both the health sector and the industrial sector since biofilm can be vector for infection to consumers beside the lowered shelf life and quality that affect the products **Wang (2019)**. The process of forming biofilms can happen through five main stages: the reversible attachment of planktonic cells, the irreversible attachment, the early development where matrix components are produced, the maturation where a three-dimensional structure is formed, and the dispersion that leads to the release of planktonic bacteria **Muhammad et al. (2020)**.

The most prevalent bacteria in biofilm formation

Pseudomonas, *Listeria*, *Enterobacter*, *Micrococcus*, *Bacillus*, *Staphylococcus*, and *Streptococcus* are all prevalent bacteria found on food contact surfaces in the dairy production industry. The most important infections to be controlled in the livestock production sector are *Staphylococcus aureus*, *Campylobacter*, *Escherichia coli* O157:H7, *Salmonella*, and *Listeria monocytogenes*. *Escherichia coli*, *Vibrio*, *Listeria monocytogenes*, *Clostridium*, *Salmonella enteritidis*, and *Staphylococcus aureus* are the principal pathogenic bacteria that require being controlled in the fish processing industry **Liu et al. (2022)**.

Human infections are detected in processing plants for food as biofilms. Growing bacteria that are capable of forming biofilm on contact surfaces such as rubber, stainless steel, polyethylene, wood, glass, and polypropylene, and rubber gloves (RG) are a major health issue because resistant biofilms can provide a persistent source of contamination **Roy et al. (2022)**.

Traditional methods for controlling biofilm

The food processing industry employs various decontamination techniques but these methods have drawbacks like chemical residues, high costs, low efficiency, and negative impacts on food products **Dhivya et al. (2022)**. These traditional methods could be classified into: physical methods as steam, superheated steam, hot water, steam pasteurization, and high-pressure cleansing are all utilized to control biofilm. Stainless steel, like all other food contact surfaces, is subject to physical cleaning procedures **Kang et al. (2021)**, chemical methods: various types of sanitizers, as well as alkaline, acidic, and neutral detergents that are employed to combat biofilms as chlorine, sodium hypochlorite, benzalkonium chloride, quaternary ammonium compounds, mixed peroxyacetic acid/organic acid, hydrogen peroxide, and peracetic acid are among the chemicals that are employed, and mechanical methods: biofilms are effectively eliminated by means of techniques involving the application of substantial mechanical force. One effective method of biofilm removal is by scrubbing or scouring the surfaces that are likely to come into contact with food **Dhivya et al. (2022)**.

Control by alternative novel methods

It is imperative to explore and develop safe and innovative approaches to effectively manage biofilm formation, the utilization of physical and chemical methods in controlling biofilm has been found to have adverse impacts on both the environment and consumers. The formation of biofilms by pathogenic and spoilage bacteria can give rise to a continuous reservoir of product contamination, resulting in significant hygienic challenges and economic losses attributed to food spoiling **Hemmati et al. (2021)**.

1. Addition of flavorzyme

Flavorzyme, an uncommon compound frequently employed as a food additive, has been deemed non-hazardous for application on all food-contact surfaces. By means of hydrolyzing a bitter peptide, this industrial peptidase is extensively employed to impart flavor to a variety of food items, including sausages, poultry meat, turkey and bovine meat, and porcine

blood **Zhang *et al.* (2019)**. In recent studies, evidence has emerged regarding the antibacterial activity of this enzyme against *Staphylococci* derived from humans **Elchinger *et al.* (2014)**.

2. Plant-based phytochemicals

Usage of Quercetin as anti-biofilm agent

Quercetin, a flavonoid found in various fruits and plants, has numerous antioxidants, free radical scavenger, anticancer, and neuroprotective properties. Its three-ring structure with 5 hydroxyl groups provides powerful antioxidant capabilities, reducing oxidative stress and limiting biofilm development. Quercetin also exhibits antibacterial effects against Gram-positive and Gram-negative bacteria, making it an effective antibiofilm agent **Roy *et al.* (2022)**.

Usage of ursolic acid as anti-biofilm agent

A natural terpenoid compound from peels of fruits, is effective against *Staphylococcus* Sp, *E. coli*, *P. aeruginosa*, and *Vibrio harveyi* biofilm formation **Jyothi *et al.* (2018)**.

Plasma-activated water

Plasma-activated water (PAW) generates reactive components at the interface of a liquid or liquid-gas medium. PAW is produced either by bringing plasma into contact with the water's surface or by using water itself. They are extremely acidic, and the chemical reactions of reactive components generate acids like nitrous acid and hydrogen peroxides. As a result, the PAW can be employed as a disinfectant. The antimicrobial efficacy of PAW is influenced by a multitude of factors, including the method, system, voltage, frequency, treatment duration, and biofilm properties. By inducing lipid oxidation, membrane disruption, and oxidative injury, plasma-activated water compromises the defense mechanism of bacterial cells **Dhivya *et al.* (2022)**.

Ultrasonication

Ultrasound, sound above 20 kHz, disrupts biofilms by creating pressure differences and cavitation. It is often combined with other treatments to increase efficacy. Combining airborne acoustic ultrasound with PAW increases biofilm removal. Ultrasound with a chelating agent and enzymes removes 75%-100% of *E. coli* and *S. aureus* biofilms in meat processing

facilities. When *Listeria monocytogenes* biofilm exposed to 35 kHz ultrasound with surfactants, it induced viable cell loss. Ultrasound at 20 kHz is more effective against *L. monocytogenes* on stainless steel surfaces when paired with 0.5 ppm ozone **Dhivya *et al.* (2022)**.

Electrolyzed oxidized water

The effects of EW on microbes and food qualities, including color and oxidation, are still being studied. This unconventional 'green' technology tries to manage microbial contamination of food without using chemical disinfectants such chlorinated water, resulting in minimal chemical/toxic residues **Tolba *et al.* (2023)**. Electrolyzed water is increasingly important in biofilm removal, by adding it to cleansing water, it prevents microbial growth, kills pathogens, and spoiling germs. EO water can be made from tap water. Electrodialysis produces electrolyzed water from diluted saline and an electrical current. Electrodialysis concentrates liquid process streams well. Electrodialysis produces two solutions by dividing the generator position between the electrodes with a membrane.

A positive anode produces acidic (pH < 3.0) EO water with O₂, HCl, HOCl, and Cl₂ **Dhivya *et al.* (2022)**. Conversely, the cathode produces alkaline ER water (pH ≥ 11.0) by reacting sodium hydroxide, hydroxyl, and sodium ions. HOCl is created when sodium chloride electrolyzes at the anode. Electrolyzed oxidized water disinfects well when ORP is larger than 1000 mv and pH is low. It can clean at high pH and ORP below 800 mv **Hassan and Dann (2019)**. Electrolyzed oxidized water reduces surface-attached bacteria by one to three logs. Electrolyzed oxidized water has been chosen by a number of organizations as a highly effective sanitizer due to containing HOCl. Electrolyzed reducing water containing NaOH is regarded as cleaner. In order to prevent contamination and deterioration of food products and preserve their quality and safety, the food industry typically employs sanitizers. The popularity of this subject can be attributed to its straightforward production and implementation. The majority of manufacturers utilize this mechanism to produce Electrolyzed oxidized water that is simple to manipulate, potentially facilitating the production of food

products free from microorganisms **Hussien *et al.* (2018).**

Electrolysis produces electrolyzed oxidized water with potent antimicrobial properties against a wide range of microorganisms. Electrolyzed oxidized water is environmentally friendly and did not influence the organoleptic properties of food. The efficacy of Electrolyzed oxidized water is directly correlated to exposure conditions, concentration and duration of exposure, inactivating pathogens and reducing contamination caused by microorganisms **Salisbury and Percival (2018).**

The consequences of consuming food with antibiotic-resistant genes for human health.

It has been reported that antibiotic-resistant strains that emerge in animals as a result of overuse or random use of antimicrobial agents may be capable of transmitting to humans **Kardomatea (2022).** There are several harmful impacts of antibiotic residues in foods such as the transfer of antibiotic resistance between MDR and commensal bacteria, which may contribute to imbalance of gut microbiota, harming human health **De Mesquita Souza Saraiva *et al.* (2021).**

Antibiotic use creates selective pressure on the microbial population; the more antibiotics used, the greater this pressure. A growing number of infections have developed resistance to one or more of the antimicrobial drugs used to treat them **Kardomatea (2022).** This issue increases when antimicrobials are consumed inappropriately **De Mesquita Souza Saraiva *et al.* (2021).** Even when antibiotics are used properly, a few cells may survive and transfer resistance characteristics, resulting in multi-antibiotic-resistant bacteria **Samtiya *et al.* (2022).**

The risks of treatment failure and increased morbidity and mortality associated with antibiotic-resistant infections.

AMR bacteria can be transmitted indirectly through food or directly by contact with sick animals or biological materials (blood, feces, urine, saliva, semen, and other body fluids). The development of antibiotic-resistant pathogens poses an important risk to the general population due to a lack of innovative antibiotics; the number of effective therapies against multi-antibiotic-resistant bacteria are limited, allowing AMR bacteria to multiply **Samtiya *et***

***al.* (2022).**

The significance of interdisciplinary collaborations and international cooperation in combating antibiotic resistance.

To reduce the prevalence of ARB and ARGs, antibiotic use must initially be curbed. the U.S. FDA has developed rules to reduce the use of antibiotics as dietary supplements for animals to improve growth and protection **Manson *et al.* (2019).** WHO has also developed plans to reduce the use of antibiotics and to establish a certain percentage of middle-income and low-income countries **Qamar *et al.* (2023).**

Many strategies to Mitigate Antibiotic Resistance; the current initiatives and regulations aimed at reducing antibiotic use in animal agriculture, the alternative approaches diminish the antibiotic resistance, the importance of accountability in antibiotic use and strict control measures should be applied through food chain as strict control of factories and control of all stages of manufacturing **Moghimi *et al.* (2023),** Follow-up the safe storage of feed and ensure the cleanliness of animal litter used as fertilizer **Alam *et al.* (2020),** attention to contaminated water drains **Hayward *et al.* (2020),** and use MALDI-TOF as a tool to recognize the causes of food-borne illness in a short time to control microbiological hazards in food-stuffs **Khater *et al.* (2021).**

This article illuminates the ways in which antibiotic resistance genes can spread through various sources in the animal environment, including water, soil, and equipment. It underscores the important role these sources have in the transfer of antibiotic-resistant bacteria (ARB) to animals, and subsequently to consumers via the food chain. The research presented in the article highlights the necessity for a collaborative approach among healthcare professionals, veterinarians, policymakers, and the agricultural sector to effectively address antibiotic resistance.

Moreover, the review highlights the importance of understanding the resistance mechanisms used by bacteria, whether they are intrinsic or acquired, and how these mechanisms influence antibiotic resistance. It also investigates the development of biofilms on surfaces that come into contact with food by food-borne bacteria and the implications for food safety and quality.

Conclusion

Antibiotic resistance transmitting through food is a growing concern due to the selective pressure of antibiotics on microbial populations. This resistance can be intrinsic or acquired, allowing bacteria to survive and protect themselves. Factors contributing to antibiotic resistance include inappropriate or excessive use of antimicrobials, global travel, poor sanitation, and non-digested antibiotic leakage into the environment. The transmission of antibiotic-resistant genes through food is a significant concern, necessitating further research, surveillance, and effective strategies to mitigate the spread of these genes through food.

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