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Review

Antimicrobial resistance in food-associated *Escherichia coli* in Mexico and Latin America

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The World Health Organization (WHO) considers antimicrobial resistance to be one of the critical global public health priorities to address. *Escherichia coli* is a commensal bacterium of the gut microbiota in humans and animals; however, some strains cause infections and are resistant to antibiotics. One of the most common ways of acquiring pathogenic *E. coli* strains is through food. This review analyzes multidrug-resistant *E. coli* isolated from food, emphasizing Latin America and Mexico, and the mobile genetic elements (MGEs) responsible for spreading antibiotic resistance determinants among bacteria in different environments and hosts. We conducted a systematic search of the literature published from 2015 to 2022 in open access databases and electronic repositories. The prevalence of 11 *E. coli* pathotypes was described, with diarrheagenic *E. coli* pathotypes being the most frequently associated with foodborne illness in different Latin American countries, highlighting the presence of different antibiotic resistance genes mostly carried by IncF-type plasmids or class 1 integrons. Although the global incidence of foodborne illness is high, there have been few studies in Mexico and Latin America, which highlights the need to generate updated epidemiological data from the "One Health" approach, which allows monitoring of the multidrug-resistance phenomenon in *E. coli* from a common perspective in the interaction of human, veterinary, and environmental health.

Key words: food, *Escherichia coli*, antimicrobial resistance, Mexico, Latin America

INTRODUCTION

Bacterial resistance to antibiotics has a serious impact on public health, which is why the World Health Organization (WHO) considers it one of the critical priorities to be addressed. Foodborne illnesses are the set of diseases caused by the ingestion of food and/or water containing etiological agents in sufficient quantities to affect the health of the consumer. These diseases are characterized by a wide variety of symptoms, such as diarrhea, vomiting, abdominal pain, headache, nausea, and fever; in some cases, there are severe complications, such as sepsis, meningitis, miscarriage, hemolytic uremic syndrome, Reiter's syndrome, Guillain–Barré syndrome, or even death [1]. About 250 pathogens have been described that affect humans through contaminated food and beverages. It is estimated that 420,000 people die every year from consuming contaminated food and that 550 million people suffer from diarrheal diseases, of which 230,000 die each year [2]. The etiology of foodborne diseases is varied; viruses, parasites, and bacteria may be involved, with the main agents responsible for mortality being *Norovirus*, *Campylobacter* spp, *Salmonella enterica, Salmonella* Typhi, *Taenia solium, Staphylococcus aureus, Clostridium perfringens, Shigella* sp, *Listeria monocytogenes,* hepatitis A virus, and *Escherichia coli* (mainly O157:H7) [2]. The latter, being part of the intestinal microbiota, is an important indicator of fecal contamination; its detection in the environment is used to monitor the prevalence,

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types, and movement of resistance genes within and between clinical, agricultural, food, community, and environmental settings [3, 4]. It is estimated that 85% of infections caused by *E. coli* are transmitted through food by the fecal-oral route, with cattle and the products or by-products obtained from them being one of the main reservoirs that contaminate food and the environment. This contamination happens through the elimination of the pathogen in their feces, spreading between animals by direct contact, through drinking troughs, shared feed, contaminated grazing sites, or other environmental sources [5].

This review aims to provide an update on the involvement of *E. coli* pathotypes in the development of foodborne diseases as well as the wide range of genetic mechanisms that the bacterium uses to resist the effects of antimicrobials, highlighting the potential for transfer of these determinants through mobile or mobilizable genetic elements. The importance of approaching this phenomenon from the "One Health" point of view, a current approach promoted by the WHO to comprehensively address and contain the spread of the disease, and containing the spread of multidrug-resistant (MDR) bacteria in a comprehensive manner is also discussed.

MATERIALS AND METHODS

A systematic search of the literature was carried out to identify recent bibliographic citations reporting the association of *E. coli* in the development of foodborne illness as well as the mechanisms of resistance to antibiotics most frequently used to treat infections caused by the bacterium. The search was initially performed in the PubMed database, using the following keywords: "*Escherichia coli* in foodborne diseases", "*Escherichia coli* pathotypes and foodborne diseases", "Antimicrobial resistance in *Escherichia coli*", "Mechanisms of antibiotic resistance in *Escherichia coli*", "Horizontal genetic transference of resistance genes in *Escherichia coli*", and "Genetic elements carrying antimicrobial resistance genes in *Escherichia coli*". In order to obtain studies reported in Mexico and Latin America, we also used the Google Scholar search engine and the following keywords: "Foodborne diseases in Mexico", "ETA in Mexico", "Foodborne diseases in Latin America", "Foodborne diseases in Latin America", "*Escherichia coli* isolated from food", "*Escherichia coli* isolated from food in Mexico", "*Escherichia coli* isolated from food in Latin America", "Mechanisms of antibiotic resistance in *Escherichia coli*", and "Dissemination of antimicrobial resistance in *Escherichia coli*". A total of 220 articles were retrieved. The articles were selected based on the following criteria: a) to address epidemiological data on foodborne diseases and their associations with *E. coli*, b) to describe virulence determinants in diarrheagenic and extraintestinal pathotypes of *E. coli*, c) to characterize *E. coli* strains isolated from food, d) to determine antibiotic resistance genes in enterobacteria and *E. coli*, and e) to describe the mechanisms and elements of genetic material transfer. This review did not generate data that had to be recorded in repositories with an accession number.

RESULTS

A total of 95 articles and 4 electronic repositories from educational and health institutions were included, which were limited to a publication and/or update period from 2015 to 2022.

Pathotypes of E. coli *associated with foodborne diseases in Mexico and Latin America*

Among the most frequent infections caused by *E. coli* are enteric and diarrheal diseases. Foodborne diarrheagenic pathotypes of *E. coli* produce virulence factors (VFs) encoded by several important genes widely reported around the world (Table 1) [6, 7]. The group of diarrheagenic pathotypes is composed of enteropathogenic *E. coli* (EPEC), Shiga toxin-producing *E. coli*/ enterohemorrhagic *E. coli* (STEC/EHEC), enteroinvasive *E. coli* (EIEC), enteroaggregative *E. coli* (EAEC), enterotoxigenic *E. coli* (ETEC), and diffusely adherent *E. coli* (DAEC) [6, 8]; STEC, one of the most important pathogens causing foodborne diseases, includes *E. coli* O157:H7. Serogroups other than O157 (O26, O45, O103, O111, O121, and O145) are known as non-O157 STEC serogroups and are also related to foodborne diseases. Transmission of an STEC causing infections occurs mainly via the consumption or handling of contaminated food, such as raw or undercooked minced meat products, raw milk, raw vegetables, contaminated raw sprouted seeds, and contact with infected animals [6, 9]. However, although the pathotypes mentioned are highly related to foodborne diseases, there are intestinal pathotypes that have shown severe intestinal involvement, such as adherent-invasive *E. coli* (AIEC). AIEC is a pathotype with particular importance in the last decades due to its frequent presence in patients with Crohn's disease and ulcerative colitis, which are commonly referred to as inflammatory bowel disease (IBD), and is a relevant pathotype because it is an intestinal bacterium with severe clinical implications [10, 11]. Extraintestinal pathogenic *E. coli* (ExPEC) diseases can cause a wide variety of infections at multiple anatomic sites. This group includes uropathogenic *E. coli* (UPEC), neonatal meningitis *E. coli* (NMEC), sepsis-associated *E. coli* (SEPEC), avian pathogenic *E. coli* (APEC), and a potentially emerging ExPEC lineage called endometrial pathogenic *E. coli* (EnPEC) [12]. ExPEC possess multiple virulence traits and genes (Supplementary Table 1) [12–15], which allow them to invade and adapt to body sites outside the gastrointestinal tract on any surface, such as food products, especially raw meats [13]. The transmission capacity of ExPEC strains is considered to be of great importance due to the variety of diseases they cause. Neonatal meningitis caused by NMEC strains is one of the most common infections, and it contributes to a neonatal mortality rate of 10% and a morbidity rate of 30% [14]. UPEC is one of the main causes of nosocomial infections and community-acquired urinary tract infections [16]. In Mexico alone, 549,984 cases of urinary tract infections have been reported so far in 2023 [17], with *E. coli* being the main etiological agent. Although these infections are treatable, the increase in MDR bacteria among ExPEC strains represents a major challenge , as it implies an increase in health care costs and leads to complications, drug treatment failures, as well as higher morbidity and mortality rates [18].

In Latin America, at least 77 million people get ill each year from consuming contaminated food, up to 9,000 people die each year, and 10–17 cases per 100,000 are children under 5 years of age who manifest hemorrhagic colitis or sporadic infection with enterotoxin-producing *E. coli*. Although *E. coli* is generally considered harmless to humans, certain pathogenic strains can infect the intestinal area and cause severe disease [6]. Studies in different Latin American countries (Table 2) [1, 7, 19–22] have indicated differences in the prevalence of various pathotypes of

E. coli. For example, in Colombia and Nicaragua, most of the reported cases of diarrhea are associated with ETEC, while in Argentina, Mexico, Brazil, Paraguay, and Peru, the most frequent pathotype is EAEC; on the other hand, in Chile, Venezuela, and Uruguay, the main associated pathotype is EPEC [23].

Mexico, like many developing countries, experiences a high incidence of foodborne diseases caused by diarrheagenic strains of *E. coli* found in different foods. These strains show high resistance to first-line antibiotics [22]. In 2017, the General Director of Inocuidad Agroalimentaria, Acuícola y Pesquera del Servicio Nacional de Sanidad e Inocuidad y Calidad Agroalimentaria (SENASICA) reported that 16,000 people die every year due to foodborne diseases in the country [24]. In Mexico, more than 120,000 cases of intestinal infectious diseases have been reported [25], with diarrheal diseases being the second most common cause of morbidity in children under five years of age, with a mortality rate of 27.78 per 100,000 in children under one year of age and 3.47 per 100,000 in children between one and four years of age [26]. *E. coli* infections are mainly transmitted through food, such as undercooked ground meat, raw milk, salads, leeks, raw potatoes, vegetables, fruits, and other foods [6] often associated with poor hygienic conditions. According to the WHO list of priority antibiotic resistant pathogens published in 2017, *E. coli* resistant to carbapenems and 3rd generation cephalosporins, as well as extended-spectrum beta-lactamase (ESBL) producers, is among the pathogens of critical priority or first attention, as it has acquired resistance to a high number of antibiotics and can cause severe and often lethal infections [9].

Table 1. Intestinal pathotypes of *E. coli* and their main virulence factors

Pathotype	Clinical symptoms	Host	Virulence factor	Virulence gene	Location	References
EHEC/ STEC	Non-bloody diarrhea, abdominal pain, fever and vomiting	Ruminants (bovine), adults, children	Shiga toxin Intimin Enterohemolysin	*stx1*, *stx2* *eae* *E-hly(ehxA)*	Phage Locus LEE Plasmid	[6, 7]
EAEC	Watery diarrhea with bloodless mucus	Adults, children, travelers to developing countries	AAF/I-V (Fimbriae) Transcriptional Activator Pet (protease SPATE) EAST1 Mucinase	*aggA, aafA, agg3A-5A* *aggR* *pet* *astA* *pic*	Plasmid/ Chromosome	[6, 7]
EPEC	Acute diarrhea, abdominal pain, vomiting and fever	Children <5 years old, adults with high inoculums	Bundlin Intimin Enterohemolysin	*bfpA* *eae* *E-hly(ehxA)*	Plasmid Locus LEE Plasmid	[6, 7]
ETEC	Acute watery diarrhea	Children <5 years old, adults, immunocompromised, travelers	Heat-stable toxin Heat-labile toxin EAST1	*est* *elt* *asta*	Plasmid/ Chromosome	[6]
EIEC	Dysentery Watery diarrhea	Children <5 years old, adults, immunocompromised, travelers	Invasin A Antigen H	*invA* *ipaH*	Plasmid INV	[6]
DAEC	Watery diarrhea without blood	Humans	Adhesin F1845	*daaC*	Plasmid/ Chromosome	[6, 7]

EHEC: enterohemorrhagic *E. coli*; STEC: Shiga toxin-producing *E. coli*; EAEC: enteroaggregative *E. coli*; EPEC: enteropathogenic *E. coli*; ETEC: enterotoxigenic *E. coli*; EIEC: enteroinvasive *E. coli*; DAEC: diffusely adherent *E. coli.*

Table 2. Reports of foodborne *E. coli* in Latin American countries

Country	Finding	References
Argentina	The STEC pathotype is endemic in Argentina with a prevalence of approximately 500 cases per year and an incidence of 12 to 14 cases per 100,000 in children under five years of age.	[19]
Colombia	Total prevalence of *E. coli* of 36.8% (28/76): Meats: 42% (16/38 samples) where 1/16 are STEC and vegetables 31% (12/38 samples) where 1/12 are STEC and 1/12 are EAEC.	[1]
Paraguay	The frequency of pathotypes in pediatric patients is: 34% ETEC, 22% EAEC, 23% EPEC, 15% EIEC, 4% STEC and 3 2% ETEC/EAEC, 0.5% ETEC/EAEC/EIEC.	[20]
Peru	In 3,284 *E. coli* strains isolated from pediatric patients in eight previous studies atypical EPEC (54/74, 73%) was the most frequent pathotype.	[21]
Venezuela	The frequency of diarrheogenic *E. coli* is 18.9%, with EPEC being the most frequently isolated pathotype, followed by ETEC and EIEC, while EAEC strains are in last place.	[7]
Costa Rica	The prevalence of diarrheogenic *E. coli* is 8.4% corresponding to EPEC.	[21]
Mexico	The frequency of diarrheogenic strains was 23%; EAEC was the most commonly isolated category, followed by EPEC and ETEC (12.2%, 5.1% and 4.3%, respectively).	[22]

STEC: Shiga toxin-producing *E. coli*; ETEC: enterotoxigenic *E. coli*; EAEC: enteroaggregative *E. coli*; EPEC: enteropathogenic *E. coli*; EIEC: enteroinvasive *E. coli*; STEC: Shiga toxin-producing *E. coli*.

E. coli *genome and genetic plasticity*

The complete genome of *E. coli* ranges from 4.6 to 5.9 million base pairs and contains 4,200 to 5,500 genes. The enormous plasticity of its genome has allowed it to adapt to diverse ecological niches, the intestinal environment, and extraintestinal body sites, reflecting the great genetic diversity within the species and causing a wide spectrum of diseases. Unlike other organisms, *E. coli* has mechanisms to improve its gene pool, such as a) changes in the nucleotide sequence of the genome (mutations), b) genome remodeling through recombination, and c) acquisition of exogenous genes through horizontal gene transfer (HGT). In addition, it is estimated that 10–16% of the *E. coli* chromosome arose through HGT events, greatly facilitating its genetic flexibility and providing accessory genetic elements, such as those for antibiotic resistance or VFs [27, 28].

Due to the ability that *E. coli* possesses to exchange genetic material with other bacterial species, it has become an ideal candidate for the study of resistance gene reservoirs in distinct niches [3]. Most *E. coli* strains enter environments and ecosystems through anthropogenic activities, discharge from livestock and poultry production, hospital and municipal wastewater, or direct contact with livestock, poultry, food-producing animals, and this consequently facilitates the transfer of resistance from non-pathogenic to pathogenic strains in the same environment [4, 5], which makes community and sanitary infections caused by *E. coli* of greater concern and importance than toxigenic and diarrheal strains with high mortalities in various populations around the world [3].

Study of the easy adaptation, environmental changes, and genomic diversity that characterize *E. coli* requires the analysis of its genetic environment and the MGEs associated with VFs and antibiotic resistance genes, which could provide helpful information at the epidemiological and medical levels [4].

DISCUSSION

Antimicrobial resistance in E. coli *isolated from food in Mexico and Latin America*

In recent years, interest in antimicrobial resistance in *E. coli* isolated from food in Mexico and Latin America has increased not only because of the presence of pathogenic *E. coli* in food but also because of commensal strains with multidrug resistance worldwide. These commensal strains can act as reservoirs of resistance genes that can be shared with other resident or pathogenic microorganisms in mixed infections and contribute to treatment failure, highlighting the need to implement monitoring and control strategies for these threats [7, 29].

The high frequency of antibiotic-resistant *E. coli* in food, clinical, community, and environmental settings worldwide has been mainly attributed to the excessive and inappropriate use of antibiotics in human and veterinary medicine. Despite the strategies implemented for the prudent use of antimicrobials, both in livestock production and in the clinical area, for many years, the percentages of MDR bacteria have remained high, representing a constant therapeutic challenge [3, 30, 31]. Furthermore, the appearance of MDR *E. coli* with high virulence potential is alarming given the risk it represents for human health through the food chain. The increasing evidence of antibiotic resistance genes in diarrheagenic strains (Supplementary Table 2) [32–38] and ExPEC has seriously complicated the treatment of infections, since the presence of resistance genes in MGEs increases the possibility of spreading antibiotic resistance among STEC bacteria and other bacteria associated with foodborne diseases but also minimizes the possible therapeutic options for human infections [39, 40]. In Mexico, a high rate of resistance to quinolones has been observed in clinical, environmental, diarrheagenic, and pediatric isolates. Multidrug resistance has even been found in UPEC; however, the lack of sufficient data on the virulence spectrum and isolates from community and hospital infections makes infection control and management difficult [16]. Even so, unlike reports on clinical isolates and although the global incidences of foodborne diseases are high, there are few studies on food in Mexico and Latin America, which demonstrates the importance of generating updated data in order to provide useful information to maximize the potential impact of food-borne infections.

Mechanisms of antibiotic resistance in E. coli

Pathogenic strains of *E. coli* can harbor VFs and antibiotic resistance genes in the same MGEs facilitating their dissemination among isolates, as well as commensal strains that promote the evolution of resistance to different antibiotic families and eventually act as a gene reservoir conferring a high prevalence of resistance genes among foodborne zoonotic pathogens [30, 39, 40]. Pathogenic strains recovered from food and cases of diarrhea and food poisoning come to possess high rates of resistance to groups of commonly used antibiotics, such as quinolones, aminoglycosides, macrolides, cephalosporins, sulfonamides, fluoroquinolones, and tetracycline, with the genes *qnr*, *dfrA1*, bla_{SHV}, bla_{TEM-1}, bla_{CTX-M}, *tet*A, *tet*B, *aac (6)-Ib*, *sul*, *cat-1*, *cmlA*, and *aadA1* being the most commonly found in diarrheagenic strains, food, water, and some livestock animals, which is why resistance to antibiotics used in animals can be transmissible to humans through contact with or consumption of animal products [32–36].

In Latin America, resistance to beta-lactams is the most reported resistance mechanism, followed by resistance to quinolones [41]. Several studies have shown the presence of ESBL-producing *E. coli* in food sources such as meat and dairy products [38], as well as β-lactamase AmpC in beef and pork [33, 34]. Although the most commonly found beta-lactamases in *E. coli* are TEM, SHV, CTX-M, OXA, and NDM [42], studies in Latin America show a high persistence of the bla_{TEM-1} gene in diarrheagenic strains (Supplementary Table 2). However, genes such as bla_{CMY}, bla_{SHV}, bla_{OXA}, bla_{CTX-M}, bla_{NDM}, and bla_{TEM-1} have been identified in strains isolated from meat for human consumption and the feces of animals and encoded in different mobilizable genetic elements (Tables 3 and 4) [34, 43–62]. As mentioned above, resistance to quinolones is the second most reported resistance mechanism in Latin America, with *aac(6')-Ib-cr* and *qnr* genes being the most frequently found [41]. However, genes belonging to the chromosomal resistance mechanism, such as *gyrA* and *parC* [36], have also been identified in diarrheagenic strains isolated from meat or animals (Supplementary Table 2 and Table 3).

Mechanisms of resistance to antibiotics of last therapeutic resort

Other resistance mechanisms that have been described in *E. coli* isolates include resistance to fosfomycin caused by mutations in genes of the *glpT* o *uhpA/T* transporters [42] and by the inactivation of fosfomycin by fosfomycin-modifying

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Table 3. Plasmids related to antimicrobial resistance of *E. coli* reported in Latin American countries

Plasmid	Gene that disseminates	Sample origin	Study country	References
IncF	bla_{CMY}, bla_{SHV}, $bla_{OXA\text{-}1\text{-}like}$, $bla_{CTX\text{-}M}$ *tet*A, *tet*B, *aac(6')-Ib, sul2, sul3, aadA, cmlA, qepA, dfr2*	Pig feces and soil Human	Brazil Argentina	[43, 44]
IncFII	$bla_{CTX\text{-}M\text{-}15}$, $bla_{NDM\text{-}1}$	Human	Mexico	[45]
IncX1	$bla_{CTX\text{-}M}$, *sul3, qnrB, dfr*A12, *cmlA1*	Poultry cloacal swabs	Cuba	[46]
IncFIA	$bla_{CTX\text{-}M\text{-}15}$, bla_{CMY}, bla_{SHV}, $bla_{OXA\text{-}1\text{-}like}$, *tet*A, *tet*B, *aac(6')-Ib, aadA, sul1, sul2, sul3, floR, cmlA*	Pig feces and soil Clinical isolate	Brazil Mexico	[44, 47]
IncFIB	$bla_{TEM\text{-}1}$ *mcr-1, floR, aac(6')-Ib-cr, aadA1*, *aadA5, tet*A, *tet*B, *cat*, *qnr, dfr*A, *sul1, sul2, strA, strB,* $bla_{CTX\text{-}M\text{-}15}$, $bla_{SHV\text{-}12}$	Clinical isolate	Colombia Mexico	[47, 48]
IncI1	$bla_{CTX\text{-}M\text{-}14}$, $bla_{TEM\text{-}1}$	Clinical isolate Chicken, beef and pork meat	Uruguay Brazil	[43, 49]
IncR	$bla_{CTX\text{-}M}$, *qnrS, tet*A, *dfr*A14, *gyrA, parC, strB*	Poultry cloacal swabs	Cuba	[46]
IncI2	*mcr-1.5*	Human	Argentina	[43]
IncHI2	$bla_{CTX\text{-}M\text{-}2}$, $bla_{TEM\text{-}1}$, *sul1, aac(6')-Ib-cr, tet*A, *tet*B, *qnrB, dfr*A12, *gyrA, parC*	Chicken meat Poultry cloacal swabs	Brazil Cuba	[43, 46]
IncX2	*qnrB19, tet*A	Chicken	Paraguay	[50]
IncA / C	$bla_{CMY\text{-}2}$ $bla_{NDM\text{-}1}$	Cattle, pig, turkey, human, horse	Chile Honduras Colombia	[43, 51]
IncN	bla_{CMY}, bla_{SHV}, $bla_{OXA\text{-}1\text{-}like}$, *tet*A, *tet*B, *aadA, sul2, qnrB10, aac(6')-Ib-cr*	Pig feces and soil Human	Brazil Argentina	[43, 44]
IncX4	*mcr-1*	Chicken meat Human Food	Brazil	[52]
ColE-Like	*qnrB19*	Human	Peru Bolivia	[43]

enzymes such as FosA, FosB, FosC, or FosL. The *fosA* gene and its different subtypes have been found to be associated with plasmids in strains of *E. coli* and the Enterobacteriaceae family, with the *fosA* gene being the most commonly found in human and food-producing animal isolates [63].

In addition to fosfomycin resistance, the clinical efficacy of colistin, an antibiotic used as a last resort in the treatment of multidrug-resistant infections, was compromised by the emergence of the plasmid-mediated gene family expressing colistin resistance, comprising the *mcr-1* to *mcr-9* genes, in the last 4 years [64]. The most worrying characteristics of the *mcr* genes are their localization in transferable plasmids, because these plasmids facilitate their dissemination by conjugation between different bacterial species, and their constant co-localization with genes encoding ESBL and plasmid AmpC [48, 65]. Currently, the *mcr-1* gene has been identified in *E. coli* isolates in humans and in various foods of animal origin, including meat from chickens, pigs, piglets, cattle, calves, and turkeys [42].

In Latin America, the *mcr-1*, *mcr-3* and *mcr-5* genes have been reported in strains isolated from animals, food, and humans, in contrast to other countries, with the *mcr-2*, *mcr-3*, *mcr-4*, *mcr-5* genes having been reported in Asian and European countries and the *mcr-9* gene having been reported in the USA [66].

Genetic elements involved in the mobilization of resistance genes

As mentioned above, HGT involves the mobilization of genetic elements between bacteria in response to the stress of rapid bacterial adaptation. HGT is one of the main mechanisms responsible for the acquisition of resistance genes and an important factor in bacterial evolution. Elements such as transposons and integrons are involved in intracellular mobility between chromosomes and replicons, while plasmids, bacteriophages, or integrative conjugative elements (ICE) are involved in intercellular gene exchange. According to Latin American reports, plasmids, integrons, transposons, and insertion sequences (ISs) are the main genetic mobilization elements observed in *E. coli* (Tables 3 and 4). Studies done in other non-Latin American countries (mainly European) also show a wide distribution of resistance determinants in foodborne *E. coli* around the world (Supplementary Table 3) [3, 4, 50, 53, 63, 65, 67–93].

Plasmids

With a determinant role in the dissemination of antibiotic resistance, plasmids have the capacity to be transmitted horizontally in an autonomous way or can be mobilized. Besides being dispensable when they no longer possess genes indispensable for their host, plasmids that confer multi-resistance are normally large (>50 Kb) and conjugative and possess mechanisms that control the number of plasmid copies, regulating their replication rate [43]. The identification of plasmid characteristics provides important knowledge for understanding the contribution and acquisition of new resistance genes through MGEs as well as their ability to replicate in a wide range of hosts, making them perfect vectors for the propagation of MDR bacteria. Currently, *E. coli* strains carrying multidrug resistance plasmids are one of the most critical and worrisome antibiotic resistance problems, as they encode resistance to β-lactams, quinolones, aminoglycosides, tetracyclines, sulfonamides, and many other classes of drugs, causing ineffective treatments [28].

Table 4. Integrons, transposons, and insertion sequences associated to antimicrobial resistance genes in *E. coli* reported in Latin American countries

Genetic element	Rearrangement of genes that disseminate	Sample origin	Study country	References
Integrons				
Class 1 and 2	*aacA4-catB3-dfrA1*, *aadA1*, *dfrA1*, *aadB*, *aacC*, *dfrA17*	Chicken Clinical isolate	Mexico	[53, 54]
Class 1 and 2	*dfrA12-orfF-aadA28*, *dfrA17-aadA5*, *dfrA29*, *aadA7*, *aadA29*, *dfrA12-orfF-aadA2-cmlA-aadA1*, *dfrA1-sat2-aadA30*	Canine isolates	Brazil	[55]
Class 1 and 2	*cat1*, *dfrA1*, bla_{TEM-1}, *tet*A, *tet*B, *aac(6)-Ib*	Cattle and swine	Chile	[34]
Class 1	*dfrA17, aadA5, sul1, sul2, sul3*	Clinical isolate	Uruguay	[56]
Class 1	*aadA1b*, *aadA2*, *aadA11cΔ*, *dfrB3-aadA1di-catB2-aadA6k*	Biopurification	Argentina	[53]
Transposons				
Tn*6242*	*sul1*, *mphA*, *mphR*	Clinical isolate	Mexico	[47]
Tn*6652*	$bla_{CTX-M-14}$, bla_{TEM-1}	Clinical isolate	Uruguay	[49]
Tn*5387*	*qnrB19*	Human	Peru Bolivia	[43]
Tn*3000*	bla_{NDM-1}	ND	Brazil	[51]
Tn*4401*	bla_{KPC}	Clinical isolate	Argentina, Chile Brazil	[51, 57, 58]
Tn*125* and Tn*5393*	bla_{NDM-1}	ND	Colombia	[51]
Tn*3*	*mcr -5.3*	Horse	Brazil	[59]
Insertion sequences				
IS*Apl1*-IS30	*mcr-1*	Clinical isolate Wild Animal Production Animals Human	Colombia Argentina Mexico Bolivia	[60]
IS1	ND	Human	Argentina Colombia	[61]
IS26	ND $bla_{CTX-M-8}$, $bla_{CTX-M-15}$	Human Public wastewater treatment plants	Argentina Brazil	[61, 62]
ISEcp1-IS10	$bla_{CTX-M-14}$	Clinical isolate	Uruguay	[49]

ND: Not described.

Among the most frequently reported plasmids in *E. coli* of food origin are IncFII, IncFIB, and IncI1 isolated from animals for human consumption, such as chickens and pigs [94]. However, studies in Latin America have reported a great diversity of plasmid groups, such as IncI1, IncFIB, IncFIA, IncFIC, IncHI2, IncQ1, IncFII, IncN, IncR, IncX1, IncX4, IncA/C, IncK, IncP, IncHI1, IncI2, IncColE, and IncY, isolated from food, production animals, pork, chicken meat, and raw vegetables [52, 63].

Integrons

Gene dissemination can also be regulated by integrons capable of integrating and expressing antibiotic resistance genes. Due to variations in the amino acid sequences of their integrases, there are five classes of "mobile" integrons associated with antibiotic resistance: class 1, class 2, class 3, class 4, and class 5 integrons [95]. Class 1 and 2 integrons are frequently detected and well characterized among bacteria belonging to the *Enterobacteriaceae* family, including *E. coli*, with the first three classes of integrons being the most involved in the acquisition of the MDR phenotype [96]. Class 1 and 2 integrons have been found in plasmids and transposons, and class 3 integrons have only been found in plasmids and have generally been recovered from clinical contexts; on the other hand, class 4 integrons, or "superintegrons", and class 5 integrons have minor roles in antibiotic resistance [95].

Studies in different countries around the world have found the presence of integrons in foods such as raw meats, seafood products, fresh vegetables, and fresh fruits, indicating the presence of class 1 integrons as one of the most abundant in strains of *E. coli* isolated from food products. Class 1 and 2 integrons have been identified in research in the livestock sector and on poultry farms, and class 1, 2, and 3 integrons have been identified in poultry, fruits and vegetables, with the *dfrA1* and *aadA1* genes being the most reported in food products [53].

In Latin America, class 1 and 2 integrons have been reported (Table 4) with various origins. In Mexico, food of animal origin and fecal samples from domestic animals, humans, and wild animals have been shown to be potential sources of class 1 and 2 integrons [53, 97–99]. In Argentina, class 1 integrons have been identified in STEC strains isolated from food, animals, and the agricultural environment [32], and in Chile, class 1 and 2 integrons have been identified in strains of porcine origin [34].

Transposons

Just as plasmids play an important role in the mobilization of genes between cells, transposons, or "jumping genes", are one of the main mobile elements of dissemination due to their ability to change position within a genome and cause insertional mutations, duplications, and rearrangements in the genome [95].

Because of their self-recombination system, transposons can transfer from one plasmid to other plasmids or from a DNA

chromosome to a plasmid and vice versa, causing great variability and giving them the ability to efficiently spread resistance/virulence genes between species, regardless of their level of genetic relatedness [28, 84].

Although most of the reported transposons are of clinical origin, their incidence and spread are potentially dangerous for future or current transmission in food, and this has not yet been sufficiently studied.

Insertion sequences

The insertion sequences are the simplest transposon elements found in prokaryotes, capable of being transposed independently in an organism [90], and play an important role in the evolution and dissemination of antimicrobial resistance genes [60]. However, like transposons, they can be found in chromosomes or plasmids, in addition to having complete or partial promoters, which are frequently located at the ends, allowing them to increase the expression of neighboring genes [51].

The precise search for these elements in different countries showed with greater frequency sequences such as IS26 and ISEcp1 in both Latin American and non-Latin American countries (Table 4 and Supplementary Table 3), related to different origins, but being significant for the prevalence and perspectives formed in each study, giving greater openness to the investigation of elements related to IS, and genes involved with these.

E. coli is one of the bacteria most commonly associated with foodborne diseases due to the ease of contamination of food when harvested or handled under minimal hygienic conditions, as well as the intrinsic capacity of the bacterium to persist and acquire virulence determinants that allow it to cause damage to susceptible hosts. In addition, it has been shown that *E. coli* pathotypes present high rates of resistance to antibiotics, which limits the therapeutic options to treat infections. In this review, studies reported in the last six years were analyzed to investigate the participation of *E. coli* in the development of foodborne diseases in Mexico and Latin America. Furthermore, this review concentrated on the contents of genes involved in resistance to different families of antibiotics used in the clinic, with special emphasis on describing those harbored in MGEs such as plasmids, integrons, transposons, and insertion sequences, which facilitate the dissemination of genes among strains of *E. coli* and other enterobacteria.

Although the global incidence of foodborne diseases is high, few studies have been carried out in Mexico and Latin America, highlighting the need to generate updated and comprehensive epidemiological data with a "One Health" approach to monitor the phenomenon of resistance in *E. coli* from a common perspective in the interaction of human, veterinary, and environmental health in order to provide more information and minimize the impacts of foodborne infections caused by MDR *E. coli*. Finally, it is hoped that this literature review will contribute to a better understanding of the current situation regarding the prevalence of antimicrobial resistant *E. coli* strains in food and their potential risk to human, veterinary, and environmental health.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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