Publisher Name: ZenToks Books
Editorial Book: Emerging Trends in Microbiology
ISBN: 978-81-958975-4-4

Chapter 1

Extended-Spectrum β -lactamase-producing *Escherichia coli* in seafood and the environment: An emerging microbial challenge

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Abstract

The ability of bacteria to resist antimicrobial agents has become a significant challenge in the contemporary world. Infections caused by antibiotic-resistant bacteria can compromise the efficacy of antimicrobial chemotherapy, leading to treatment failure and increased morbidity and mortality. Although some bacteria have the intrinsic ability to tolerate one or more drugs, resistance to multiple, clinically important antibiotics is due to the acquisition of multiple resistance genes through horizontal gene transfer (HGT). Among various classes of antibiotics, beta-lactam antibiotics have been effectively used to combat Gram-negative bacterial infections for decades. *Escherichia coli*, a significant human pathogen, has developed various mechanisms to resist β-lactam antibiotics, the most notable of which is the production of extended-spectrum β-lactamase (ESBL) enzymes that hydrolyze third-generation cephalosporins, such as cefotaxime and ceftazidime, as well as the monobactams. Although carbapenems are the drugs of choice for treating ESBL producers, the emergence of carbapenem-resistant Enterobacterales (CRE) has become a serious concern. The ESBL enzymes are very diverse, grouped into various families. SHV, TEM, CTX-M, and OXA are some of the common examples of ESBL types widely present in Enterobacterales, and the genes encoding these reside on mobile genetic elements, which allow their rapid dissemination. The isolation of ESBL-producing *E. coli* has been reported from diverse food including seafood and food production environments, emphasizing the significance of the ”One Health” approach in controlling the spread of multidrug-resistant bacteria in the food chain.

1. Introduction

Seafood constitutes an essential part of a healthy diet, as it is a rich source of protein, essential fats, iodine, vitamin D, calcium, and other essential minerals. Seafood is a perishable commodity due to its high moisture content and neutral pH, which provide a favorable habitat for the growth and multiplication of microorganisms [1, 2]. In India, estuarine and coastal waters are frequently contaminated by the activities of nearby inhabitants, such as the discharge of partially or wholly untreated sewage from nearby townships. Seafood caught from such areas acts as a vector in disseminating pathogenic and drug-resistant bacteria from the environment to the community [3].

Escherichia coli is one of the most important bacteria constituting the human and animal gut microbiome. It is of utmost significance as it aids in the synthesis of vitamin K2 and vitamin B2, contributing to the health and well-being of its host [4]. At the same time, it can also cause infections of varying intensities in all age groups. Based on pathogenicity, *E. coli* is categorized into two major groups : intestinal and extraintestinal *E. coli.*. Intestinal pathogroups include diarrheagenic *E. coli* (DEC), Shiga toxin-producing *E. coli* (STEC), Enterohemorrhagic *E. coli* (EHEC), Enteropathogenic *E. coli* (EPEC), Enterotoxigenic *E. coli* (ETEC), Enteroinvasive *E. coli* (EIEC), , Entero adherent *E. coli* (EAEC), Diffusely-adhering *E. coli* (DAEC) whereas, extraintestinal pathogenic *E. coli* are Uropathogenic *E. coli* (UPEC), Sepsis-causing *E. coli* (SEPEC) and Neonatal meningitis-associated *E. coli* (NMEC) [5–8].

Our ability to treat infectious diseases has grown significantly with the discovery of several antibiotics in the 20^{th} century. However, continuous exposure to antibiotics eventually led to the development and spread of antimicrobial resistance in bacteria. Antimicrobial resistance in human pathogenic bacteria has become a global health crisis in recent years, affecting the ability to treat infectious diseases worldwide. The resistance of bacteria to structurally different antimicrobials involves several mechanisms, such as enzymatic drug inactivation, reduced drug permeability, mutations in antibiotic targets, bacterial efflux pumps, and target alteration [9] Figure 1. There have been links between the use of antibiotics in food-producing animals and the emergence of antibiotic resistance in Enterobacterales, as well as

How To Cite: R. Prerana, C.K. Dhanush,M. Lekshmi,S.H. Kumar. *Extended-Spectrum β-lactamase-producing Escherichia coli in seafood and the environment: : An emerging microbial challenge.* In V. Kanna(Eds). Emerging Trends in Microbiology. Pages 1-12, 2025. ZenToks Books, India. ISBN: 978-81-958975-4-4

the transfer of resistant organisms to the human population or their resistance genes to human pathogens through the food chain [10]. *E. coli* is identified as one of the most dangerous antimicrobial-resistant bacteria because of its ability to easily acquire and transfer resistant genes via horizontal gene transfer, leading to the emergence of multidrug-resistant strains. Infections caused by such bacteria are difficult to cure and can be fatal. Extended-spectrum β-lactamase (ESBL)-producing *E. coli* is a concerning issue in human and animal healthcare systems, as critically important antibiotics fail to control infections caused by them [11].

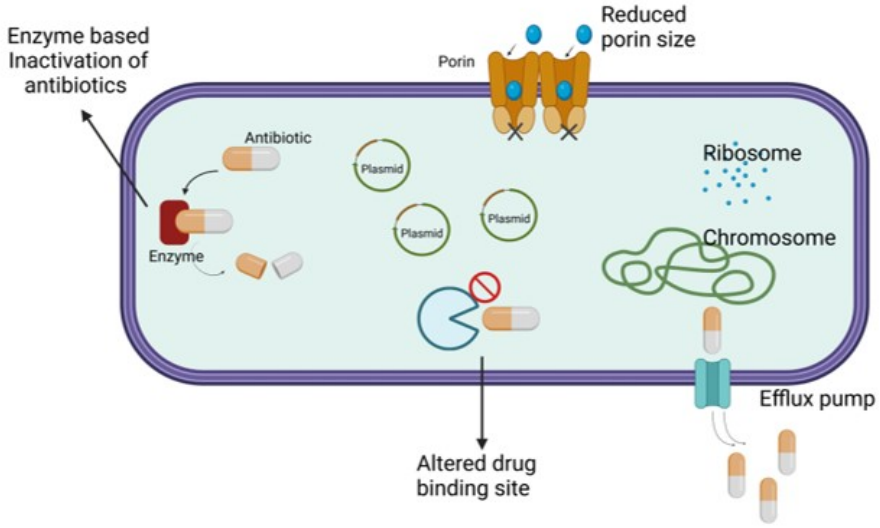

Figure 1: Bacterial mechanisms of antibiotic resistance

2. Beta-lactam antibiotics and the resistance

2.1. Beta-lactams

The discovery of antibiotics dates back more than 70 years, with Penicillin, a β-lactam class, as the first antibiotic [12]. β-lactams are the most widely used bactericidal antibiotics worldwide for human and veterinary treatment due to their effective antimicrobial properties and minimal side effects [13]. Hence, the therapeutically important antibiotics come under the β-lactam class, which comprises penicillins, cephalosporins, monobactams, and carbapenems. These antibiotics have a four-membered β-lactam ring with 3-carbon and 1-nitrogen and are distinguished by their side chain [14, 15].

Penicillin is a six-amino-penicillinic acid comprising a thiazolidine ring and a beta-lactam ring joined to a side chain. Cephalosporins are the derivatives of 7-amino-cephalosporanic acid and are structurally similar to Penicillin. Based on the chemical structures of the R1 and R2 radicals, the antibacterial and pharmacokinetic properties of cephalosporins differ. Carbapenems are five-membered rings identical to Penicillin, except that the sulphur atom at position C-1 has been substituted with a carbon atom and has a double bond between C-2 and C-3 positions. Monobactams have no adjacent ring, unlike carbapenems, cephalosporins, and Penicillin. Aztreonam is the sole agent in this class currently available. It is ineffective against gram-positive bacteria and anaerobes [15, 16] and Table 1.

2.2. Mechanism of action

β-lactams are bactericidal antibiotics that disrupt cell wall synthesis by interfering with peptidoglycan formation. β-lactams structurally imitate the D-Ala-D-Ala terminal segment of the crosslinking peptide, enabling it to covalently attach to penicillin-binding proteins (PBPs), transpeptidase enzymes involved in the terminal step of peptidoglycan synthesis in both Gram-positive and Gram-negative bacteria. This prevents the formation of bacterial cell walls, resulting in cell death [9, 14, 15, 22].

2.3. Resistance to β-lactams

Although β-lactams are considered effective antimicrobial agents, their inappropriate and overuse in agriculture, animal industry, aquaculture and healthcare has led to the development of resistance [23]. Different groups of bacteria possess different mechanism of β-lactam resistance. One of the key mechanisms involves alterations in penicillin-binding proteins (PBPs) that reduce their affinity to β-lactam antibiotics. An example of this is PBP2a in methicillin-resistant *Staphylococcus aureus* (MRSA) encoded by the mecA gene [14, 24]. Bacteria decrease the expression of or lose certain outer membrane porins that prevent β-lactam from acting at their site of action. These mutations may result in inactive or deleted porins or changes to the regulatory systems controlling them, such as OMP synthesis in Enterobacteriaceae and for *P. aeruginosa* OprD synthesis [14, 25]. Furthermore, bacteria can activate efflux pumps to eliminate antibiotics and regulate the intramembrane environment. As a result of the presence or overproduction of β-lactamases, resistance may also develop due to the overexpression of AcrAB-TolC efflux pumps in intestinal bacteria [14, 26, 27].

In Gram-negative bacteria such as *E. coli*, production of one or more β-lactamases is the most common mode of resistance. These are hydrolase enzymes that attach to the drug and break the amide bond of the four-membered lactam ring, adding a water molecule to the ring-opened molecule, thereby preventing the rebonding of the lactam ring and inhibiting the killing activity of β-lactams [14]. It shields

Table 1: List of important antibiotics belonging to different classes of the β-lactam group

β-lactam group	Subclass	Examples	Reference
Penicillins	Natural	Penicillin G, Benzathine Penicillin, Procaine Penicillin, Penicillin V	Balsalobre et al [16] Dumancas et al [17]
	Semi-natural	Methicillin, Oxacillin, Dicloxacillin, Nafcillin, Carbenicillin, Flucloxacillin, Ancillin, Phenethicillin, Propicillin, Phenbenicillin, Clometocillin, Azidocillin, Piperacillin, Azlocillin, Mezlocillin, Ticarcillin, Ampicillin, and Amoxicillin	Balsalobre et al [16] Dumancas et al [17] Rolinson & Sutherland, [18]
Cephalosporins	First-generation	Cephalothin, Cephapirin, Cefazolin, Cephalexin, Cephradine, Cefadroxil	Balsalobre et al [16] Bui et al [19]
	Second-generation	Cefamandole, Cefuroxime, Cefonicid, Cefprozil, Cefaclor, Ceforanide. Cephamycins include Cefoxitin, Cefmetazole, Cefminox, and Cefotetan.	Balsalobre et al [16] Bui et al [19] Das et al[20]
	Third-generation	Cefotaxime, Cefixime, Ceftriaxone, Ceftazidime, Ceftizoxime, Cefoperazone, Ceftibuten, Cefpodoxime and Cefdinir.	Balsalobre et al [16] Bui et al [19]
	Fourth-generation	Cefepime, Cefpirome, Cefozopran	Balsalobre et al [16] Bui et al [19] Das et al[20]
	Fifth-generation	Ceftobiprole, Ceftaroline, and Ceftolozane	Balsalobre et al [16] Bui et al [19]
Monobactams		Aztreonam	Balsalobre et al [16]
Carbapenems		Doripenem, Ertapenem, Imipenem, Biapenem, Panipenem and Meropenem	Balsalobre et al [16] Papp-Wallace et al [21]

organisms from the deadly effects of β-lactam antibiotics, such as penicillins, cephalosporins, and carbapenems, rendering them ineffective against resistant bacteria [28].

β-lactamases are broadly categorized into two major groups: serine β-lactamases (Class A, C, and D) and metal-based β-lactamases (Class B). Class A β-lactamases are abundant, among which ESBLis the most important form recorded worldwide and poses a significant threat to both the community and the environment.

3. ESBL and its dissemination

After the prevalence of penicillinases, cephalosporins are the most widely prescribed group of β-lactam antibiotics because of their mild nephrotoxicity compared to other groups of antibiotics, such as aminoglycosides and quinolones. Soon, the extensive use of cephalosporins led to the emergence of bacteria that produce extended-spectrum β-lactamases.

ESBL confers resistance to second- and third-generation cephalosporins, penicillin, and monobactams, but is inhibited by β-lactamase inhibitors, cephamycins (such as cefoxitin), and carbapenems [29]. ESBLs are serine-based β-lactamases, categorized as Ambler class A based on their molecular and structural characteristics and in group 2be of functional classification [30].

It was in the 1980s that the first ESBL was identified in Europe, with the discovery of TEM (TEM-1) and SHV (SHV-1) [31]. TEM and SHV types were the most common ESBL families in the past, with variants showing minor differences in the amino acid sequence. However, today, CTX-M type enzymes are predominant.

3.1. TEM β-lactamases

TEM stands for Temoneira. This enzyme was first discovered in *Escherichia coli* plasmid isolated from the blood of a Greek patient named Temoneira in the early 1960s. TEM type ESBLS are variations of this enzyme. The first TEM derivative, TEM-2, differs from TEM-1 β-lactamase by a single amino acid, Gln39Lys [30].

TEM-1 enzyme hydrolyzes penicillins and early cephalosporins. They are inhibited by oxyimino cephalosporins because oxyimino cephalosporins like cefotaxime and ceftazidime consist of an oxyimino side chain, which cannot be accommodated in the active site of TEM-1. R164S and G238S substitution in TEM-1 favoured oxyimino cephalosporin hydrolysis [32]. CTX-1, later termed TEM-3, had two

amino acid substitutions from TEM-1, i.e., lysine for glutamic acid at 104 residue and serine for glycine at 238 residue. TEM-3 was the first of the TEM-type variants to exhibit the ESBL phenotype identified in 1986 from the plasmids of *K. pneumoniae* in healthcare settings [33, 34]. In TEM variants, the substitution of amino acids occurs at specific, restricted sites. Among the substitutions at Arg43, Asp179, Arg205, Gly238, and Glu240, Gly238Ser and Glu240Lys tend to have the most significant influence on the development of the ESBL phenotype [35, 36]. TEM-type enzymes have become less frequent, while CTX-M β-lactamases have become the most common ESBLs globally. A fraction of a percent of ESBL-producing *E. coli* and *Klebsiella pneumoniae* were found to have TEM-type ESBLs in a recent study of European isolates [37]. In several variants, substitutions in the amino acids Asp276, Cys241, Met69, Arg241, Arg244, Arg275, and Asn276 of TEM-1 and TEM-2 resulted in resistance to β-lactamase inhibitors [38–40]. TEM-52, TEM 1, TEM-135, TEM-1P14S, TEM-3, TEM-10, and TEM-26 are the most common variants obtained worldwide [30, 41–43].

3.2. Sulfhydryl Reagent Variable (SHV) β-lactamase

Sulfhydryl reagent variable (SHV) is a type of ESBL discovered in the chromosome of *K. pneumoniae* [44]. SHV was designated so because of the perception that the inhibitory activity of SHV by p-chloromercuribenzoate was substrate-based, but this was disproved in later studies. In the 1970s, SHV-1 was the first SHV discovered in the plasmid of *E. coli*, conferring resistance to penicillins and early cephalosporins [45]. In 1983, SHV-2, a variant of SHV, was the first ESBL discovered in a *Klebsiella ozaenae* isolate from Germany, exhibiting efficient hydrolysis of cefotaxime but only marginally of ceftazidime [46]. SHV-2 varied from SHV-1 with a single amino acid substitution at position 238 from Gly to Ser. Amino acid substitution like Leu35Gln, Gly238Ser or Gly238Ala, and Glu240Arg or Glu240Lys has a crucial role in SHV ESBL phenotype [36, 45, 47]. Gly238Ser and Glu240Lys substitutions are most common in SHV ESBL types [48]. SHV-12 (22; 9%), and HV-28, SHV-5, and SHV-2a genes are the most common variants of SHV [30, 41, 45]. SHV-49, SHV-56, and SHV-107 obtained from European clinical isolates were resistant to β-lactamase inhibitors [49, 50]. However, tazobactam and avibactam are effective in inhibiting most TEM and SHV enzymes [30].

3.3. Cefotaximase β-lactamase (CTX-M)

CTX-M stands for cefotaximase from Munich, Germany, where it was first identified in a clinical isolate of *E. coli* in 1989 [51]. It was first obtained from the *E. coli* plasmid, isolated from a faecal sample of a laboratory dog treated with beta-lactams, designated as FEC-1 [52, 53]. The first clinical CTX-M isolate was obtained from the *E. coli* isolate of ear exudate of a newborn in Germany [54]. CTX-M shows only 40% similarity to TEM and SHV [55]. It was named cefotaximase because the early CTX-M versions effectively hydrolyzed cefotaxime and ceftriaxone, but had limited action against ceftazidime [52]. Later, CTX-M variants such as CTX-M-15 and CTX-M-27, which belong to the CTX-M-1 and CTX-M-9 groups, respectively, demonstrated enhanced hydrolytic activity against ceftazidime, as well as veterinary broad-spectrum cephalosporins, cefquinome, and ceftiofur [30, 31]. Asn104, Asn132, Ser237, and Asp240 residues are significant in oxyimino-cephalosporins hydrolysis [52].

CTX-M-type ESBLs are noticeably less susceptible to sulbactam's inhibitory effect than that of clavulanic acid and tazobactam, and this property helps distinguish CTX-M-type ESBL producers from TEM or SHV [31]. However, CTX-M-190 from *Escherichia coli* 70-kb IncI1 plasmid differed from CTX-M-55 with Ser133Thr substitution exhibiting resistance to sulbactam as well as tazobactam [56]. Ser237 and Arg276 substitutions play an important role in oxyimino cephalosporin hydrolysis in CTX-M bacteria with reduced β-lactamase susceptibility [55, 57].

Depending on the similarity of sequences, CTX-M is subdivided into 5 groups: CTX-M-1, CTX-M-2, CTX-M-8, CTX-M-9, and CTX-M-25 Table 2. These groups have more than 10 amino acid differences, and those with fewer than 5 amino acid differences are clustered in the same group [35, 51, 52]. CTX-M groups originate from *Kluyvera* spp, but are now seen in transferable elements [58].

Table 2: CTX-M group and the members of each cluster

CTX-M group	Members of the cluster	References
CTX-M-1	CTX-M-1, CTX-M-3 CTX-M-10, CTX-M-12 CTX-M-15, FEC-1, CTX-M-22, CTX-M-23, CTX-M-28	Bonnet et al [52] Gniadkowski et al [59] Karim et al [60] Kariuki et al [61]
CTX-M-2	CTX-M-2, CTX-M-4, CTX-M-4L, CTX-M-5, CTX-M-6, CTX-M-7, CTX-M-20, Toho-1	Bonnet et al [52]
CTX-M-8	CTX-M-8	Bonnet et al [62]
CTX-M-9	CTX-M-9, CTX-M-13 CTX-M-14, CTX-M-16, CTX-M-17, CTX-M-19, CTX-M-21, CTX-M-27, Toho-2, CTX-M-24	Bonnet et al [52]
CTX-M-25	CTX-M-25, CTX-M-26	Bonnet et al [52]

Most commonly found CTX-M enzymes are CTX-M-1, CTX-M-3, CTX-M-15, CTX-M-9, CTX-M-14, CTX-M-27, CTX-M-8, CTX-M-25 and CTX-M-2 [30, 41]. CTX-M, SHV, and TEM are the prevalent ESBL types distributed worldwide. In contrast, SFO, BES, BEL, TLA, GES, PER, and VEB are minor groups of ESBL that are endemic and sporadically detected [46, 63–67].

4. Transferability of ESBL-encoding genes

Although ESBL genes were originally reported in the chromosomes of bacteria, the extensive use of extended-spectrum beta-lactam drugs resulted in selection pressure, leading to the acquisition of these genes in mobile genetic elements, which facilitated their easy mobility and dissemination. Resistant genes are retained within transposons and insertion sequences located in plasmids, which can be easily transmitted between different bacteria. This facilitates genetic exchange processes, allowing bacterial communities to spread resistance characteristics more widely.

Insertion sequences, integrons, and transposons of family Tn3 and Tn5053 are the important mobile elements involved in the transferability of resistant genes in gram-negative bacteria [68]. The IS*26* insertion sequence, a member of the IS*6* insertion sequence, plays a crucial role in the dissemination of the *bla* gene [69]. They are mainly associated with plasmids compared to chromosomes. There are 28 plasmid incompatibility groups in the Enterobacteriaceae, with IncF, R, X, I, L/M, N, P, H, A/C, and W, which are linked to ARGs [70]. Important bla_{SHV} genes are mainly located in IncA/C, IncF, IncHI2, Incl1, IncL/M, IncN, IncX3 and IncP [45, 69]. IncP, IncQ, and IncA/C have a wide host range, and the genes present in them can be mobilised to different genera and also to gram-positive bacteria. But IncFII has a narrow host range [70–73].

The bla_{TEM} genes are carried on the transposon TnA. Based on the TEM variants, TnA is categorised into Tn*1*, Tn*2*, and Tn*3* based on the sequence difference in the res site [74]. $bla_{\text{CTX-M}}$ gene is found in the plasmids of IncN, IncI1, IncK, IncF, and IncL/M groups [71]. $bla_{\text{CTX-M}}$ gene is located in ISEcp1 or ISCR1. All members of the $bla_{\text{CTX-M}}$ groups possess IS*Ecp1*, which belongs to the IS1380 family, facilitating the easy dissemination of $bla_{\text{CTX-M}}$ genes. Of the 5 subgroups of $bla_{\text{CTX-M}}$ genes, $bla_{\text{CTX-M-2}}$ and $bla_{\text{CTX-M-9}}$ have ISCR1-like insertion sequences [60, 75, 76]. In addition, $bla_{\text{CTX-M}}$ genes are also associated with IS*10* and IS*26*, showing that the $bla_{\text{CTX-M}}$ genes are present on a wide range of mobile genetic elements [58, 77]. ISE_{cp1} was first obtained from *E. coli*, which can hold many resistant genes of varying length from different origins, conferring resistance to a wide range of antimicrobial agents [68]. Since the first discovery of plasmid-mediated bla_{TEM-1}, resistance is unstoppable for old as well as newly developed drugs, narrowing down the treatment options for deadly infections, thereby causing increased morbidity and mortality.

5. Prevalence of ESBL-producing *Escherichia coli* in seafood

Continuous use of antibiotics significantly disrupts the normal microflora, leading to the prevalence of resistant strains. However, upon withdrawal of antibiotic usage, these resistant strains diminish. But, *E. coli* O25b:H4-ST131 is an adherent-invasive *E. coli* (AIEC) that can thrive in the gut and urinary tract for a consistent period in the absence of antimicrobial pressure. Hence, the global spread of virulent *E. coli* harboring resistant genes is a challenge to physicians. An extremely potent and virulent clone from ST131 (phylogroup B2) dominates the majority of ESBL-producing *E. coli* worldwide, referred to as the "International clone" or "Epidemic strain" [31, 78, 79]. ST58 (phylogroup B1), ST167 (phylogroup A), ST393 (phylogroup D), ST1158 (phylogroup F), ST457 (phylogroup F), ST69 (phylogroup D), ST648 (phylogroup F), and ST405 (phylogroup D) are important ESBL-producing *E. coli* sequence types with global dissemination. Most ESBL *E. coli* isolates have O serogroups and H flagellar antigens [80–86].

The transboundary movement of ESBL genes was demonstrated earlier in 2012 by [87], who reported the $bla_{\text{CTX-M}}$ gene in 82% of *E. coli* isolates from imported raw frozen mackerel fish in Saudi Arabia. Antibiotic-resistant *E. coli* were isolated from frozen Pangasius fillets and shrimp imported from Asia to Denmark, that were resistant to multiple antibiotics like cephalosporins, macrolides, fluoroquinolones, and colistin [88]. Some important reports on ESBL-producing E. coli, along with resistant genes, are mentioned in Table 3.

Extended-spectrum β-lactamase (ESBL)-producing bacteria have emerged globally due to the improper use of expanded-spectrum cephalosporins to treat infections. Since then, carbapenems have been viewed as the last-resort antibiotics for treating infections caused by multidrug-resistant isolates that produce ESBL. Under the pressure of using carbapenem in therapeutic settings, various mechanisms for carbapenem resistance have emerged. Over the past decade, the lack of effective medicines and the widespread transmission of carbapenem-resistant Enterobacterales (CRE) have made this pathogen a significant threat to public health. Genes encoding extended-spectrum β-lactamases have undergone mutation, giving rise to carbapenemases that cause the most problems, leaving only a few antimicrobials effective against them [108]. Among bla_{TEM}, bla_{SHV}, and blaCTX, the $bla_{\text{SHV-38}}$ gene is the only ESBL variant that has the ability to hydrolyze carbapenems (such as imipenem). The imipenem-hydrolyzing ability of the *bla* gene was due to a point mutation from alanine to valine at the 146 Ambler position [109]. Overexpression of the bla_{CTX-M} gene and reduced porin size contribute to carbapenem resistance in Enterobacterales. Due to the loss of OmpC/OmpF in these mutants, the fitness cost explains the failure of successful emergence in clinical species [110]. The co-occurrence of ESBL and carbapenemase genes, which confer resistance to all β-lactams, highlighted the ineffectiveness of β-lactams in treatment. Furthermore, the combination of β-lactamase-producing genes with other antibiotic-resistant genes has given rise to superbugs, exacerbating the current situation. Extended-spectrum β-lactamase (ESBL)-producing bacteria have emerged globally due to the improper use of expanded-spectrum cephalosporins to treat infections. Since then, carbapenems have been viewed as the last-resort antibiotics for treating infections caused by multidrug-resistant isolates that produce ESBL. Under the pressure of using carbapenem in therapeutic settings, various mechanisms for carbapenem resistance have emerged. Over the past decade, the lack of effective medicines and the widespread transmission of carbapenem-resistant Enterobacterales (CRE) have made this pathogen a significant threat to public health. Genes encoding extended-spectrum β-lactamases have undergone mutation, giving rise to carbapenemases that cause the most problems, leaving only a few antimicrobials effective against them [108]. Among bla_{TEM}, bla_{SHV}, and blaCTX, the $bla_{\text{SHV-38}}$ gene is the only ESBL variant that has the ability to hydrolyze carbapenems (such as imipenem). The imipenem-hydrolyzing ability of the *bla* gene was due to a point mutation from alanine to valine at the 146 Ambler position [109]. Overexpression of the $bla_{\text{CTX-M}}$ gene and reduced porin size contribute to carbapenem resistance in Enterobacterales. Due to the loss of OmpC/OmpF in these mutants, the fitness cost explains the failure of successful emergence in clinical species [110]. The co-occurrence of ESBL and carbapenemase genes, which confer resistance to all β-lactams, highlighted the ineffectiveness of β-lactams in treatment. Furthermore, the combination of β-lactamase-producing genes with other antibiotic-resistant genes has given rise to superbugs, exacerbating the current situation.

Given that we are in the post-antibiotic era, preventing antibiotic resistance is no longer possible. However, reducing antibiotic usage can subsequently reduce the selection of resistant bacteria, thereby decreasing the survival and spread of resistant strains. It can be achieved by using alternatives to antibiotics for treatments, such as vaccines, monoclonal/polyclonal antibodies, bacteriophages, phytochemicals,

Table 3: Reports on ESBL-producing *E. coli* in seafood

Country	Sample	Antibiotic-resistant Genes	Reference
China	680 fish, 143 shrimp, and 26 shellfish	mcr-1, $bla_{\text{TEM-1}}$, $bla_{CTX\text{-}M\text{-}14}$, $bla_{\text{CTX-M-55}}$, *tetA*, *strA/B*, *sul2*, aadA, *floR*, and *qnrS*	Zhang et al [89]
Germany (Berlin)	160 seafood	$bla_{\text{CTX-M}}$, bla_{CMY}, or bla_{DHA}	Vu et al [90]
India (Assam)	79	*dfrA1*, *sul1*, *qnrB*, *qnrS*, *tetA*, *sul2* *aac*(6)*-Ib-cr*, $bla_{\text{CTX-M-15}}$, $bla_{\text{CMY-2}}$, bla_{SHV}, bla_{TEM}	Sivaraman et al [91]
India (Assam)	94	$bla_{\text{CTX-M-1}}$, $bla_{\text{CTX-M-9}}$, $bla_{\text{CTX-M-15}}$, $bla_{\text{CTX-M-14}}$, bla_{TEM} bla_{SHV}, *blaOXA-1*, *ydgE/F*, *sugE(c)*, *mdfA*, *emrE* gene	Sajeev et al [92]
India (Maharashtra)	37 fish and 13 shellfish	$bla_{\text{CTX-M}}$, bla_{SHV}, *blaOXA*, *blaNDM* and *blaVIM*	Singh et al [13] Dhanush et al [93]
India (Maharashtra)	14 fish, 3 shrimp, 1 squid and 1 clam	$bla_{\text{CTX-M}}$, bla_{SHV}, bla_{TEM} and *blaNDM*	Singh et al [29]
India (Tamil Nadu)	31	$bla_{\text{CTX-M}}$, bla_{TEM} bla_{SHV}, and bla_{AmpC}	Kamala & Sivaperumal [94]
India (Tamil Nadu)	44 finfish, 19 shellfish	$bla_{\text{CTX-M}}$, bla_{SHV}, bla_{TEM}, and *ampC* genes	Kavinesan et al [95]
Japan	50	$bla_{\text{CTX-M-65}}$, bla_{TEM}	Xedzro et al [96]
Nigeria	238	bla_{TEM} and *tetA*	Odumosu et al [97]
Northeast Algeria (Constantine)	100 sardines and 50 red shrimp	$bla_{\text{CTX-M-15}}$	Dib et al [98]
Northern Portugal	150	$bla_{\text{CTX-M-1}}$, bla_{TEM}, *tet(A)* and *aadA* gene	Silva et al [99]
Norway	390 bivalves	$bla_{\text{CTX-M-15}}$, $bla_{\text{CTX-M-3}}$, $bla_{\text{CTX-M-1}}$, $bla_{\text{CMY-42}}$	Svanevik et al [100]
Portugal	522 bivalves	$bla_{\text{CTX-M-32}}$, $bla_{\text{CTX-M-15}}$, $bla_{\text{CTX-M-14}}$	Freire et al [101]
South America	42	$bla_{\text{CTX-M}}$	Sellera et al [102]
Thailand	144 oyster meat	$bla_{\text{CTX-M-55}}$, bla_{TEM}, tetA	Jeamsripong et al [103]
Tunisia	70	$bla_{\text{CTX-M-1}}$	Said et al [104]
Tunisia (Sousse, Mahdia, and Monastir, Gabès)	641 pieces of sea bream and sea bass; 1075 Mediterranean clams	$bla_{\text{CTX-M-1}}$, $bla_{\text{CTX-M-15}}$, $bla_{\text{CTX-M-14}}$, $bla_{\text{CTX-M-27}}$, *tetA*, *tetB*, *dfr* genes	Sola et al [105]
Turkey	96 mussels, 96 shrimp	$bla_{\text{CTX-M}}$, bla_{TEM}	Celik et al [106]
Vietnam (Nha Trang)	60 shrimp	$bla_{\text{CTX-M-1}}$, $bla_{\text{CTX-M-9}}$, bla_{TEM}, and bla_{SHV}	Le et al [107]

antimicrobial enzymes, and peptides [111]. Several actions are undertaken globally by governments with various programs, which include the "One Health" approach, Global Antimicrobial Resistance and Use Surveillance System (GLASS), Global Action Plan for managing AMR (GAP-AMR) to narrow down the information gap in antibiotics usage and also link the health of community with that of its associated environment [112].

6. Conclusion

Seafood caught usually contains *Vibrio* spp, but the presence of *Escherichia coli* indicates the secondary contamination of seafood. One of the main reasons is the release of improperly treated domestic and hospital sewage into coastal waters. The irrelevant and illogical use of antibiotics in aquatic environments also contributes to the propagation of antibiotic resistance. Such fish acts as a reservoir of resistant genes that are transmitted to the community when eaten raw or via cross-contamination. Continuous surveillance and documentation of antibiotics from production to consumption should be maintained. The over-the-counter availability of critically important antibiotics should be controlled, and educating the general public regarding the importance of antibiotics and their resistance is a pressing need. Studies reported on ESBL-EC bacteria in seafood highlight the threat to the public, indicating their circulation between the environment and the community. Hence, policymakers should take necessary measures and implement effective management practices, such as antibiotic stewardship programs and the one health approach, in every state and district to address the issue of antibiotic resistance.

References

[1] C. Jayasekara, E. Mendis, S.-K. Kim, and P. Kim. Seafood in the human diet for better nutrition and health. *2939–2959*, 2020. doi:10.1002/9781119143802.ch131.

[2] C. Liu and N. V. C. Ralston. Seafood and health: What you need to know? *Advances in Food and Nutrition Research*, 97:275–318, 2021. doi:10.1016/bs.afnr.2021.04.001.

[3] S. Kumar, A. Parvathi, and I. Karunasagar. Prevalence and antibiotic resistance of *Escherichia coli* in tropical seafood. *World Journal of Microbiology and Biotechnology*, 21:619–623, 2005. doi:10.1007/s11274-004-3555-8.

[4] W. Al-Zyoud, A. Nasereddin, H. Aljarajrah, and M. Saket. Culturable gut bacteria lack *escherichia coli* in children with phenylketonuria. *New Microbes and New Infections*, 32:100616, 2019. doi:10.1016/j.nmni.2019.100616.

[5] V. S. Braz, K. Melchior, and C. G. Moreira. *Escherichia coli* as a multifaceted pathogenic and versatile bacterium. *Frontiers in Cellular and Infection Microbiology*, 10, 2020. doi:10.3389/fcimb.2020.548492.

[6] J. B. Kaper, J. P. Nataro, and H. L. Mobley. Pathogenic *escherichia coli*. *Nature Reviews. Microbiology*, 2(2):123–140, 2004. doi:10.1038/nrmicro818.

[7] S. Kumar, M. Lekshmi, A. Parvathi, B. Nayak, and M. Varela. Antibiotic resistance in seafood-borne pathogens. *Foodborne Pathogens and Antibiotic Resistance*, pages 397–415, 2017. doi:10.1002/9781119139188.ch17.

[8] B. Pawłowska and B. M. Sobieszczańska. Intestinal epithelial barrier: The target for pathogenic *Escherichia coli*. *Advances in Clinical and Experimental Medicine: Official Organ Wroclaw Medical University*, 26(9):1437–1445, 2017. doi:10.17219/acem/64883.

[9] M. F. Varela, J. Stephen, M. Lekshmi, M. Ojha, N. Wenzel, L. M. Sanford, A. J. Hernandez, A. Parvathi, and S. H. Kumar. Bacterial resistance to antimicrobial agents. antibiotics (basel. *Switzerland)*, 10(5):593, 2021. doi:10.3390/antibiotics10050593.

[10] M. Lekshmi, P. Ammini, S. Kumar, and M. F. Varela. The food production environment and the development of antimicrobial resistance in human pathogens of animal origin. *Microorganisms*, 5(1):11, 2017. doi:10.3390/microorganisms5010011. PMID: 28335438. PMCID: PMC5374388.

[11] V. S. Sonola, A. Katakweba, G. Misinzo, and M. I. Matee. Molecular epidemiology of antibiotic resistance genes and virulence factors in multidrug-resistant *Escherichia coli* isolated from rodents, humans, chicken, and household soils in karatu, northern tanzania. *International Journal of Environmental Research and Public Health*, 19(9), 2022. doi:10.3390/ijerph19095388. Article 9.

[12] R. N. Iyer. Beta lactam. In *Comprehensive Pharmacology*, pages 3–63. Elsevier, 2022. doi:10.1016/B978-0-12-820472-6.00212-7.

[13] A. S. Singh, B. B. Nayak, and S. H. Kumar. High prevalence of multiple antibiotic-resistant, extended-spectrum -lactamase (esbl)-producing *Escherichia coli* in fresh seafood sold in retail markets of mumbai, india. *Veterinary Sciences*, 7(2):46, 2020. doi:10.3390/vetsci7020046.

[14] K. Bush and P. A. Bradford. Epidemiology of -lactamase-producing pathogens. *Clinical Microbiology Reviews*, 33(2):e00047–19, 2020. doi:10.1128/CMR.00047-19.

[15] M. Ibrahim, U. Zango, S. A. Shawai, and I. Shamsuddin. A review on beta-lactam antibiotic drug resistance. *Drug Design, Development and Therapy*, 3:52–58, 2019.

[16] L. Balsalobre, A. Blanco, and T. Alarcón. Beta-lactams. In Antibiotic Drug Resistance, editor, *Ltd*, pages 57–72. John Wiley Sons, 2019. doi:10.1002/9781119282549.ch3.

[17] G. G. Dumancas, R. S. Hikkaduwa Koralege, E.-R. E. Mojica, B. S. Murdianti, and P. J. Pham. Penicillins. In *Encyclopedia of Toxicology*, pages 768–772. Elsevier, 2014. doi:10.1016/B978-0-12-386454-3.00764-8.

[18] G. N. Rolinson and R. Sutherland. Semisynthetic penicillins. In *Advances in Pharmacology (Vol. 11)*, pages 151–220. Elsevier, 1973. doi:10.1016/S1054-3589(08)60458-5.

[19] T. Bui, P. Patel, and C. V. Preuss. Cephalosporins. In *StatPearls*. StatPearls Publishing, 2024. http://www.ncbi.nlm.nih.gov/books/NBK551517/.

[20] N. Das, J. Madhavan, A. Selvi, and D. Das. An overview of cephalosporin antibiotics as emerging contaminants: A serious environmental concern. *3 Biotech*, 9(6):231, 2019. doi:10.1007/s13205-019-1766-9.

[21] K. M. Papp-Wallace, A. Endimiani, M. A. Taracila, and R. A. Bonomo. Carbapenems: Past, present, and future . *Antimicrobial Agents and Chemotherapy*, 55(11):4943–4960, 2011. doi:10.1128/AAC.00296-11.

[22] N. Pandey and M. Cascella. Beta-lactam antibiotics. In *StatPearls*. StatPearls Publishing, 2024. http://www.ncbi.nlm.nih.gov/books/NBK545311/.

[23] S. Wall. Prevention of antibiotic resistance—an epidemiological scoping review to identify research categories and knowledge gaps. *Global Health Action*, 12(1):1756191, 2019. doi:10.1080/16549716.2020.1756191.

[24] M. E. Fergestad, G. A. Stamsås, D. Morales Angeles, Z. Salehian, Y. Wasteson, and M. Kjos. Penicillin-binding protein pbp2a provides variable levels of protection toward different -lactams in *Staphylococcus aureus* rn4220. *MicrobiologyOpen*, 9(8):e1057, 2020. doi:10.1002/mbo3.1057.

[25] G. Zhou, Q. Wang, Y. Wang, X. Wen, H. Peng, R. Peng, Q. Shi, X. Xie, and L. Li. Outer membrane porins contribute to antimicrobial resistance in gram-negative bacteria. *Microorganisms*, 11(7):1690, 2023. doi:10.3390/microorganisms11071690.

[26] A. Sharma, V. K. Gupta, and R. Pathania. Efflux pump inhibitors for bacterial pathogens: From bench to bedside. *The Indian Journal of Medical Research*, 149(2):129–145, 2019. doi:10.4103/ijmr.IJMR_2079_17.

[27] S. M. Soto. Role of efflux pumps in the antibiotic resistance of bacteria embedded in a biofilm. *Virulence*, 4(3):223–229, 2013. doi:10.4161/viru.23724.

[28] G. Muteeb, M. T. Rehman, M. Shahwan, and M. Aatif. Origin of antibiotics and antibiotic resistance, and their impacts on drug development: A narrative review. *Pharmaceuticals*, 16(11):1615, 2023. doi:10.3390/ph16111615.

[29] A. Sanjit Singh, M. Lekshmi, S. Prakasan, B. B. Nayak, and S. Kumar. Multiple antibiotic-resistant, extended spectrum--lactamase (esbl)-producing enterobacteria in fresh seafood. *Microorganisms*, 5(3):53, 2017. doi:10.3390/microorganisms5030053.

[30] M. Castanheira, P. J. Simner, and P. A. Bradford. Extended-spectrum -lactamases: An update on their characteristics, epidemiology and detection. *JAC-Antimicrobial Resistance*, 3(3), 2021. doi:10.1093/jacamr/dlab092. dlab092.

[31] K. Kawamura, N. Nagano, M. Suzuki, J.-I. Wachino, K. Kimura, and Y. Arakawa. ESBL-producing *Escherichia coli*. 2017.

[32] T. Palzkill. Structural and mechanistic basis for extended-spectrum drug-resistance mutations in altering the specificity of tem, CTX-M, and kpc -lactamases. *Frontiers in Molecular Biosciences*, 5, 2018. doi:10.3389/fmolb.2018.00016.

[33] C. Brun-Buisson, A. Philippon, M. Ansquer, P. Legrand, F. Montravers, and J. Duval. Transferable enzymatic resistance to third-generation cephalosporins during nosocomial outbreak of multiresistant *KLEBSIELLA PNEUMONIAE*. *The Lancet*, 330(8554): 302–306, 1987. doi:10.1016/S0140-6736(87)90891-9.

[34] W. Sougakoff, S. Goussard, G. Gerbaud, and P. Courvalin. Plasmid-mediated resistance to third-generation cephalosporins caused by point mutations in tem-type penicillinase genes. *Clinical Infectious Diseases*, 10(4):879–884, 1988. doi:10.1093/clinids/10.4.879.

[35] P. A. Bradford. Extended-spectrum beta-lactamases in the 21st century: Characterization, epidemiology, and detection of this important resistance threat. *Clinical Microbiology Reviews*, 14(4):933–951, 2001. doi:10.1128/CMR.14.4.933-951.2001. table of contents.

[36] J. R. Knox. Extended-spectrum and inhibitor-resistant tem-type beta-lactamases: Mutations, specificity, and three-dimensional structure. *Antimicrobial Agents and Chemotherapy*, 39(12):2593–2601, 1995. doi:10.1128/aac.39.12.2593.

[37] K. M. Kazmierczak, B. L. M. de Jonge, G. G. Stone, and D. F. Sahm. Longitudinal analysis of ESBL and carbapenemase carriage among enterobacterales and *Pseudomonas aeruginosa* isolates collected in europe as part of the international network for optimal resistance monitoring (inform) global surveillance programme, 2013–17. *Journal of Antimicrobial Chemotherapy*, 75(5):1165–1173, 2020. doi:10.1093/jac/dkz571.

[38] A. Belaaouaj, C. Lapoumeroulie, M. M. Caniça, G. Vedel, P. Névot, R. Krishnamoorthy, and G. Paul. Nucleotide sequences of the genes coding for the tem-like beta-lactamases irt-1 and irt-2 (formerly called tri-1 and tri-2). *FEMS Microbiology Letters*, 120(1-2): 75–80, 1994. doi:10.1111/j.1574-6968.1994.tb07010.x.

[39] C. Henquell, C. Chanal, D. Sirot, R. Labia, and J. Sirot. Molecular characterization of nine different types of mutants among 107 inhibitor-resistant tem beta-lactamases from clinical isolates of escherichia coli. *Antimicrobial Agents and Chemotherapy*, 39(2): 427–430, 1995. doi:10.1128/AAC.39.2.427.

[40] A. Philippon, P. Slama, P. Dény, and R. Labia. A structure-based classification of class a -lactamases, a broadly diverse family of enzymes. *Clinical Microbiology Reviews*, 29(1):29, 2016. doi:10.1128/CMR.00019-15.

[41] H. Ejaz, S. Younas, K. O. A. Abosalif, K. Junaid, B. Alzahrani, A. Alsrhani, A. E. Abdalla, M. I. Ullah, M. U. Qamar, and S. S. M. Hamam. Molecular analysis of blashv, blatem, and blactx-m in extended-spectrum -lactamase producing enterobacteriaceae recovered from fecal specimens of animals. *PLOS ONE*, 16(1):e0245126, 2021. doi:10.1371/journal.pone.0245126.

[42] T. A. Elsener, K. A. Jolley, E. Sanders, M. C. J. Maiden, A. Cehovin, and C. M. Tang. There are three major neisseria gonorrhoeae -lactamase plasmid variants which are associated with specific lineages and carry distinct tem alleles. *Microbial Genomics*, 9(7): 001057, 2023. doi:10.1099/mgen.0.001057.

[43] M. E. Ibrahim, T. B. Algak, M. Abbas, and B. K. Elamin. Emergence of *bla*tem, *bla*ctx-m, *bla* SHV and *bla*oxa genes in multidrug-resistant *Enterobacteriaceae* and *Acinetobacter baumannii* in saudi arabia. *Experimental and Therapeutic Medicine*, 22(6):1–11, 2021. doi:10.3892/etm.2021.10885.

[44] D. M. Livermore. Beta-lactamases in laboratory and clinical resistance. *Clinical Microbiology Reviews*, 8(4):557–584, 1995. doi:10.1128/CMR.8.4.557.

[45] A. Liakopoulos, D. Mevius, and D. Ceccarelli. A review of SHV extended-spectrum -lactamases: Neglected yet ubiquitous. *Frontiers in Microbiology*, 7, 2016. doi:10.3389/fmicb.2016.01374.

[46] D. L. Paterson and R. A. Bonomo. Extended-spectrum beta-lactamases: A clinical update. *Clinical Microbiology Reviews*, 18(4): 657–686, 2005. doi:10.1128/CMR.18.4.657-686.2005.

[47] M. T. Nüesch-Inderbinen, F. H. Kayser, and H. Hächler. Survey and molecular genetics of SHV beta-lactamases in enterobacteriaceae in switzerland: Two novel enzymes, SHV-11 and SHV-12. *Antimicrobial Agents and Chemotherapy*, 41(5):943–949, 1997. doi:10.1128/AAC.41.5.943.

[48] A. Huletsky, J. R. Knox, and R. C. Levesque. Role of ser-238 and lys-240 in the hydrolysis of third-generation cephalosporins by SHV-type beta-lactamases probed by site-directed mutagenesis and three-dimensional modeling. *The Journal of Biological Chemistry*, 268(5):3690–3697, 1993.

[49] V. Dubois, L. Poirel, C. Arpin, L. Coulange, C. Bebear, P. Nordmann, and C. Quentin. SHV-49, a novel inhibitor-resistant -lactamase in a clinical isolate of *Klebsiella pneumoniae*. *Antimicrobial Agents and Chemotherapy*, 48(11):4466–4469, 2004. doi:10.1128/AAC.48.11.4466-4469.2004.

[50] N. Mendonça, E. Ferreira, D. Louro, Participants Arsip, and M. Caniça. Molecular epidemiology and antimicrobial susceptibility of extended- and broad-spectrum beta-lactamase-producing klebsiella pneumoniae isolated in portugal. *International Journal of Antimicrobial Agents*, 34(1):29–37, 2009. doi:10.1016/j.ijantimicag.2008.11.014.

[51] G. Peirano and J. D. D. Pitout. Molecular epidemiology of *Escherichia coli* producing CTX-M -lactamases: The worldwide emergence of clone st131 o25:h4. *International Journal of Antimicrobial Agents*, 35(4):316–321, 2010. doi:10.1016/j.ijantimicag.2009.11.003.

[52] R. Bonnet. Growing group of extended-spectrum -lactamases: The CTX-M enzymes. *Antimicrobial Agents and Chemotherapy*, 48(1): 1–14, 2004. doi:10.1128/AAC.48.1.1-14.2004.

[53] Y. Matsumoto, F. Ikeda, T. Kamimura, Y. Yokota, and Y. Mine. Novel plasmid-mediated beta-lactamase from*Escherichia coli* that inactivates oxyimino-cephalosporins. *Antimicrobial Agents and Chemotherapy*, 32(8):1243–1246, 1988.

[54] A. Bauernfeind, H. Grimm, and S. Schweighart. A new plasmidic cefotaximase in a clinical isolate of escherichia coli. *Infection*, 18 (5):294–298, 1990. doi:10.1007/BF01647010.

[55] L. S. Tzouvelekis, E. Tzelepi, P. T. Tassios, and N. J. Legakis. CTX-M-type beta-lactamases: An emerging group of extended-spectrum enzymes. *International Journal of Antimicrobial Agents*, 14(2):137–142, 2000. doi:10.1016/s0924-8579(99)00165-x.

[56] Z. Shen, B. Ding, Y. Bi, S. Wu, S. Xu, X. Xu, Q. Guo, and M. Wang. CTX-M-190, a novel -lactamase resistant to tazobactam and sulbactam, identified in an *Escherichia coli* clinical isolate. *Antimicrobial Agents and Chemotherapy*, 61(1):e01848–16, 2016. doi:10.1128/AAC.01848-16.

[57] M. Gazouli, N. J. Legakis, and L. S. Tzouvelekis. Effect of substitution of asn for arg-276 in the cefotaxime-hydrolyzing class a beta-lactamase CTX-M. *FEMS Microbiology Letters*, 169(2):289–293, 1998. doi:10.1111/j.1574-6968.1998.tb13331.x.

[58] M. M. D'Andrea, F. Arena, L. Pallecchi, and G. M. Rossolini. CTX-M-type -lactamases: A successful story of antibiotic resistance. *International Journal of Medical Microbiology*, 303(6):305–317, 2013. doi:10.1016/j.ijmm.2013.02.008.

[59] M. Gniadkowski, I. Schneider, A. Pałucha, R. Jungwirth, B. Mikiewicz, and A. Bauernfeind. Cefotaxime-resistant enterobacteriaceae isolates from a hospital in warsaw, poland: Identification of a new CTX-M-3 cefotaxime-hydrolyzing -lactamase that is closely related to the CTX-M-1/men-1 enzyme. *Antimicrobial Agents and Chemotherapy*, 42(4):827–832, 1998.

[60] A. Karim, L. Poirel, S. Nagarajan, and P. Nordmann. Plasmid-mediated extended-spectrum beta-lactamase (CTX-M-3 like) from india and gene association with insertion sequence isecp1. *FEMS Microbiology Letters*, 201(2):237–241, 2001. doi:10.1111/j.1574-6968.2001.tb10762.x.

[61] S. Kariuki, J. E. Corkill, G. Revathi, R. Musoke, and C. A. Hart. Molecular characterization of a novel plasmid-encoded cefotaximase (CTX-M-12) found in clinical klebsiella pneumoniae isolates from kenya. *Antimicrobial Agents and Chemotherapy*, 45(7):2141–2143, 2001. doi:10.1128/AAC.45.7.2141-2143.2001.

[62] R. Bonnet, J. L. M. Sampaio, R. Labia, C. De Champs, D. Sirot, C. Chanal, and J. Sirot. A novel CTX-M -lactamase (CTX-M-8) in cefotaxime-resistant enterobacteriaceae isolated in brazil. *Antimicrobial Agents and Chemotherapy*, 44(7):1936–1942, 2000.

[63] E. Akinci and H. Vahaboglu. Minor extended-spectrum -lactamases. *Expert Review of Anti-Infective Therapy*, 8(11):1251–1258, 2010. doi:10.1586/eri.10.119.

[64] A. Bauernfeind, I. Stemplinger, R. Jungwirth, P. Mangold, S. Amann, E. Akalin, O. Anğ, C. Bal, and J. M. Casellas. Characterization of beta-lactamase gene blaper-2, which encodes an extended-spectrum class a beta-lactamase. *Antimicrobial Agents and Chemotherapy*, 40(3):616–620, 1996. doi:10.1128/AAC.40.3.616.

[65] T. Naas, L. Poirel, and P. Nordmann. Minor extended-spectrum -lactamases. *Clinical Microbiology and Infection*, 14:42–52, 2008. doi:10.1111/j.1469-0691.2007.01861.x.

[66] S. Sánchez-Urtaza, A. Ocampo-Sosa, A. Molins-Bengoetxea, J. Rodríguez-Grande, M. A. El-Kholy, M. Hernandez, D. Abad, S. M. Shawky, I. Alkorta, and L. Gallego. Co-existence of blandm-1, blaoxa-23, blaoxa-64, blaper-7 and blaadc-57 in a clinical isolate of acinetobacter baumannii from alexandria, egypt. *International Journal of Molecular Sciences*, 24(15):12515, 2023. doi:10.3390/ijms241512515.

[67] L. Xie, J. Wu, F. Zhang, L. Han, X. Guo, Y. Ni, and J. Sun. Molecular epidemiology and genetic characteristics of various blaper genes in shanghai, China. *Antimicrobial Agents and Chemotherapy*, 60(6):3849–3853, 2016. doi:10.1128/aac.00258-16.

[68] S. R. Partridge. Analysis of antibiotic resistance regions in gram-negative bacteria. *FEMS Microbiology Reviews*, 35(5):820–855, 2011. doi:10.1111/j.1574-6976.2011.00277.x.

[69] J. Mahillon and M. Chandler. Insertion sequences. *Microbiology and Molecular Biology Reviews*, 62(3):725–774, 1998. doi:10.1128/mmbr.62.3.725-774.1998.

[70] A. Carattoli, A. Bertini, L. Villa, V. Falbo, K. L. Hopkins, and E. J. Threlfall. Identification of plasmids by pcr-based replicon typing. *Journal of Microbiological Methods*, 63(3):219–228, 2005. doi:10.1016/j.mimet.2005.03.018.

[71] A. Carattoli. Plasmids and the spread of resistance. *International Journal of Medical Microbiology: IJMM*, 303(6-7):298–304, 2013. doi:10.1016/j.ijmm.2013.02.001.

[72] A. El Salabi, T. R. Walsh, and C. Chouchani. Extended spectrum -lactamases, carbapenemases and mobile genetic elements responsible for antibiotics resistance in gram-negative bacteria. *Critical Reviews in Microbiology*, 39(2):113–122, 2013. doi:10.3109/1040841X.2012.691870.

[73] S. R. Partridge, S. M. Kwong, N. Firth, and S. O. Jensen. Mobile genetic elements associated with antimicrobial resistance. *Clinical Microbiology Reviews*, 31(4):10, 2018. doi:10.1128/cmr.00088-17. 1128/cmr. 00088-17.

[74] S. R. Partridge and R. M. Hall. Evolution of transposons containing blatem genes. *Antimicrobial Agents and Chemotherapy*, 49(3): 1267–1268, 2005. doi:10.1128/aac.49.3.1267-1268.2005.

[75] L. Poirel, M.-F. Lartigue, J.-W. Decousser, and P. Nordmann. Isecp1b-mediated transposition of blactx-m in *Escherichia coli*, journal = Antimicrobial Agents and Chemotherapy, volume = 49, number = 1, pages = 447-450, note = doi:10.1128/AAC.49.1.447-450.2005.,. 2005.

[76] W.-H. Zhao and Z.-Q. Hu. Epidemiology and genetics of CTX-M extended-spectrum -lactamases in gram-negative bacteria. *Critical Reviews in Microbiology*, 39(1):79–101, 2013. doi:10.3109/1040841X.2012.691460.

[77] A. Cullik, Y. Pfeifer, R. Prager, H. von Baum, and W. Witte. A novel is*26* structure surrounds blactx-m genes in different plasmids from German clinical *Escherichia coli* isolates. *Journal of Medical Microbiology*, 59(Pt 5):580–587, 2010. doi:10.1099/jmm.0.016188-0.

[78] A. Giedraitienė, A. Vitkauskienė, A. Pavilonis, V. Patamsytė, N. Genel, D. Decre, and G. Arlet. Prevalence of o25b-st131 clone among escherichia coli strains producing CTX-M-15, CTX-M-14 and CTX-M-92 -lactamases. *Infectious Diseases (London, England)*, 49(2): 106–112, 2017. doi:10.1080/23744235.2016.1221531.

[79] M. Martinez-Medina, A. Mora, M. Blanco, C. López, M. P. Alonso, S. Bonacorsi, M.-H. Nicolas-Chanoine, A. Darfeuille-Michaud, J. Garcia-Gil, and J. Blanco. Similarity and divergence among adherent-invasive *Escherichia coli* and extraintestinal pathogenic *E. coli* strains. *Journal of Clinical Microbiology*, 47(12):3968–3979, 2009. doi:10.1128/JCM.01484-09.

[80] A. Belas, C. Marques, J. Menezes, L. T. da Gama, P. Cavaco-Silva, and C. Pomba. Esbl/pampc-producing escherichia coli causing urinary tract infections in non-related companion animals and humans. *Antibiotics*, 11(5):559, 2022. doi:10.3390/antibiotics11050559.

[81] R. Dziri, N. Klibi, C. A. Alonso, A. Jouini, L. Ben Said, S. Chairat, R. Bellaaj, A. Boudabous, K. Ben Slama, and C. Torres. Detection of CTX-M-15-producing *Escherichia coli* isolates of lineages st131-b2 and st167-a in environmental samples of a tunisian hospital. *Microbial Drug Resistance (Larchmont, N. Y.)*, 22(5):399–403, 2016. doi:10.1089/mdr.2015.0354.

[82] R. Mamani, S. C. Flament-Simon, V. García, A. Mora, M. P. Alonso, C. López, I. García-Meniño, D. Díaz-Jiménez, J. E. Blanco, M. Blanco, and J. Blanco. Sequence types, clonotypes, serotypes, and virotypes of extended-spectrum -lactamase-producing *Escherichia coli* causing bacteraemia in a spanish hospital over a 12-year period (2000 to 2011). *Frontiers in Microbiology*, 10, 2019. doi:10.3389/fmicb.2019.01530.

[83] K. Nesporova, E. R. Wyrsch, A. Valcek, I. Bitar, K. Chaw, P. Harris, J. Hrabak, I. Literak, S. P. Djordjevic, and M. Dolejska. *Escherichia coli* sequence type 457 is an emerging extended-spectrum--lactam-resistant lineage with reservoirs in wildlife and food-producing animals. *Antimicrobial Agents and Chemotherapy*, 65(1):e01118–20, 2020. doi:10.1128/AAC.01118-20.

[84] Â. Novais, C. Vuotto, J. Pires, C. Montenegro, G. Donelli, T. M. Coque, and L. Peixe. Diversity and biofilm-production ability among isolates of *Escherichia coli*phylogroup d belonging to st69, st393 and st405 clonal groups. *BMC Microbiology*, 13(1):144, 2013. doi:10.1186/1471-2180-13-144.

[85] C. J. Reid, M. L. Cummins, S. Börjesson, M. S. M. Brouwer, H. Hasman, A. M. Hammerum, L. Roer, S. Hess, T. Berendonk, K. Nešporová, M. Haenni, J.-Y. Madec, A. Bethe, G. B. Michael, A.-K. Schink, S. Schwarz, M. Dolejska, and S. P. Djordjevic. A role for colv plasmids in the evolution of pathogenic *Escherichia coli* st58. *Nature Communications*, 13(1):683, 2022. doi:10.1038/s41467-022-28342-4.

[86] P. Roy Chowdhury, J. McKinnon, M. Liu, and S. P. Djordjevic. Multidrug resistant uropathogenic *Escherichia coli* st405 with a novel, composite is26 transposon in a unique chromosomal location. *Frontiers in Microbiology*, 9:3212, 2018. doi:10.3389/fmicb.2018.03212.

[87] N. Elhadi and K. Alsamman. Incidence and antimicrobial susceptibility pattern of extended-spectrum--lactamase-producing *Escherichia coli* isolated from retail imported mackerel fish. *African Journal of Biotechnology*, 14(23), 2015. doi:10.5897/AJB2015.14698. Article 23.

[88] J. Ellis-Iversen, A. M. Seyfarth, H. Korsgaard, V. Bortolaia, N. Munck, and A. Dalsgaard. Antimicrobial resistant *E. coli* and enterococci in pangasius fillets and prawns in danish retail imported from asia. *Food Control*, 114:106958, 2020. doi:10.1016/j.foodcont.2019.106958.

[89] S. Zhang, Y. Huang, G. Yang, Q. Wu, J. Zhang, J. Wang, Y. Ding, Y. Su, Q. Ye, S. Wu, Q. Gu, X. Wei, and Y. Zhang. High prevalence of multidrug-resistant *Escherichia coli* in retail aquatic products in China and the first report of mcr-1-positive extended-spectrum -lactamase-producing *E. coli* st2705 and st10 in fish. *International Journal of Food Microbiology*, 408:110449, 2024. doi:10.1016/j.ijfoodmicro.2023.110449.

[90] T. T. T. Vu, T. Alter, U. Roesler, N. Roschanski, and S. Huehn. Investigation of extended-spectrum and ampc -lactamase–producing enterobacteriaceae from retail seafood in berlin, germany. *Journal of Food Protection*, 81(7):1079–1086, 2018. doi:10.4315/0362-028X.JFP-18-029.

[91] G. K. Sivaraman, S. Sudha, K. H. Muneeb, B. Shome, M. Holmes, and J. Cole. Molecular assessment of antimicrobial resistance and virulence in multi drug resistant ESBL -producing *Escherichia coli* and klebsiella pneumoniae from food fishes, assam, india. *Microbial Pathogenesis*, 149:104581, 2020. doi:10.1016/j.micpath.2020.104581.

[92] S. Sajeev, M. Hamza, V. Rajan, A. Vijayan, G. K. Sivaraman, B. R. Shome, and M. A. Holmes. Resistance profiles and genotyping of extended-spectrum beta-lactamase (esbl) -producing and non-esbl-producing *E. coli* and klebsiella from retail market fishes. *Infection, Genetics and Evolution*, 112:105446, 2023. doi:10.1016/j.meegid.2023.105446.

[93] C. K. Dhanush, M. Lekshmi, S. K. Girisha, B. B. Nayak, and S. H. Kumar. Quinolone and colistin resistance genes in extended-spectrum beta-lactamase (esbl)-producing *Escherichia coli* of diverse phylogenetic groups isolated from seafood in mumbai, india. *Applied Microbiology*, 5(1):3, 2025. doi:10.3390/applmicrobiol5010003.

[94] K. Kamala and P. Sivaperumal. Predominance of multidrug resistant extended spectrum lactamase producing bacteria from marine fishes. *Environmental Pollution*, 323:121314, 2023. doi:10.1016/j.envpol.2023.121314.

[95] K. Kavinesan, G. Sugumar, B. Chrisolite, A. Muthiahsethupathy, S. Sudarshan, F. Parthiban, and M. Mansoor. Phenotypic and genotypic characterization of pathogenic *escherichia coli* identified in resistance mapping of -lactam drug-resistant isolates from seafood along tuticorin coast. *Environmental Science and Pollution Research*, 30(26):68111–68128, 2023. doi:10.1007/s11356-023-27008-y.

[96] C. Xedzro, T. Shimamoto, and T. Shimamoto. Predominance of multidrug-resistant gram-negative bacteria isolated from supermarket retail seafood in japan. *Microorganisms*, 11(12), 2023. doi:10.3390/microorganisms11122935. Article 12.

[97] B. T. Odumosu, H. I. Obeten, and T. A. Bamidele. Incidence of multidrug-resistant*Escherichia coli* harbouring blatem and teta genes isolated from seafoods in lagos nigeria. *Current Microbiology*, 78(6):2414–2419, 2021. doi:10.1007/s00284-021-02511-y.

[98] A. L. Dib, A. Agabou, A. Chahed, C. Kurekci, E. Moreno, M. Espigares, and E. Espigares. Isolation, molecular characterization and antimicrobial resistance of enterobacteriaceae isolated from fish and seafood. *Food Control*, 88:54–60, 2018. doi:10.1016/j.foodcont.2018.01.005.

[99] V. Silva, J. Nunes, A. Gomes, R. Capita, C. Alonso-Calleja, J. E. Pereira, C. Torres, G. Igrejas, and P. Poeta. Detection of antibiotic resistance in *Escherichia coli* strains: Can fish commonly used in raw preparations such as sushi and sashimi constitute a public health problem? *Journal of Food Protection*, 82(7):1130–1134, 2019. doi:10.4315/0362-028X.JFP-18-575.

[100] C. S. Svanevik, M. Norström, B. T. Lunestad, J. S. Slettemeås, and A. M. Urdahl. From tide to table: A whole-year, coastal-wide surveillance of antimicrobial resistance in *Escherichia coli* from marine bivalves. *International Journal of Food Microbiology*, 407: 110422, 2023. doi:10.1016/j.ijfoodmicro.2023.110422.

[101] S. Freire, T. Grilo, B. Rodrigues, R. Oliveira, C. Esteves, A. Marques, L. Poirel, and M. Aires-de Sousa. ESBL- and carbapenemase-producing *Escherichia coli* and klebsiella pneumoniae among bivalves from portuguese shellfish production areas. *Microorganisms*, 11(2), 2023. doi:10.3390/microorganisms11020415. Article 2.

[102] F. P. Sellera, M. R. Fernandes, Q. Moura, M. P. N. Carvalho, and N. Lincopan. Extended-spectrum--lactamase (CTX-M)-producing *Escherichia coli* in wild fishes from a polluted area in the atlantic coast of south america. *Marine Pollution Bulletin*, 135:183–186, 2018. doi:10.1016/j.marpolbul.2018.07.012.

[103] S. Jeamsripong, M. Kuldee, V. Thaotumpitak, and R. Chuanchuen. Antimicrobial resistance, extended-spectrum -lactamase production and virulence genes in salmonella enterica and escherichia coli isolates from estuarine environment. *PLOS ONE*, 18(4):e0283359, 2023. doi:10.1371/journal.pone.0283359.

[104] L. B. Said, M. Hamdaoui, A. Jouini, A. Boudabous, K. B. Slama, C. Torres, and N. Klibi. First detection of CTX-M-1 in extended-spectrum -lactamase–producing *Escherichia coli* in seafood from tunisia. *Journal of Food Protection*, 80(11):1877–1881, 2017. doi:10.4315/0362-028X.JFP-16-324.

[105] M. Sola, Y. Mani, E. Saras, A. Drapeau, R. Grami, M. Aouni, J.-Y. Madec, M. Haenni, and W. Mansour. Prevalence and characterization of extended-spectrum -lactamase- and carbapenemase-producing enterobacterales from tunisian seafood. *Microorganisms*, 10(7), 2022. doi:10.3390/microorganisms10071364. Article 7.

[106] B. Celik, B. Ergul, A. I. Kekec, B. Hala, B. Maslak, B. D. Sigirci, B. B. Kahraman, A. F. Bagcigil, K. Metiner, and S. Ak. Beta-lactam, aminoglycoside, and quinolone resistance in *Escherichia coli* strains isolated from shrimps and mussels in the marmara sea. *Veterinární Medicína*, 68(5):208–217, 2023. doi:10.17221/105/2022-VETMED.

[107] Q. P. Le, S. Ueda, T. N. H. Nguyen, T. V. K. Dao, T. A. Van Hoang, T. T. N. Tran, I. Hirai, T. Nakayama, R. Kawahara, T. H. Do, Q. M. Vien, and Y. Yamamoto. Characteristics of extended-spectrum -lactamase–producing *Escherichia coli* in retail meats and shrimp at a local market in vietnam. *Foodborne Pathogens and Disease*, 12(8):719–725, 2015. doi:10.1089/fpd.2015.1954.

[108] L. Poirel, J.-Y. Madec, A. Lupo, A.-K. Schink, N. Kieffer, P. Nordmann, and S. Schwarz. Antimicrobial resistance in *Escherichia coli*. *Microbiology Spectrum*, 6(4), 2018. doi:10.1128/microbiolspec.ARBA-0026-2017.

[109] L. Poirel, C. Héritier, I. Podglajen, W. Sougakoff, L. Gutmann, and P. Nordmann. Emergence in *Klebsiella pneumoniae* of a chromosome-encoded SHV -lactamase that compromises the efficacy of imipenem. *Antimicrobial Agents and Chemotherapy*, 47(2): 755–758, 2003. doi:10.1128/aac.47.2.755-758.2003.

[110] M. Adler, M. Anjum, D. I. Andersson, and L. Sandegren. Influence of acquired -lactamases on the evolution of spontaneous carbapenem resistance in *Escherichia coli*. *The Journal of Antimicrobial Chemotherapy*, 68(1):51–59, 2013. doi:10.1093/jac/dks368.

[111] R. Gupta and S. Sharma. Role of alternatives to antibiotics in mitigating the antimicrobial resistance crisis. *The Indian Journal of Medical Research*, 156(3):464–477, 2022. doi:10.4103/ijmr.IJMR_3514_20.

[112] K. W. K. Tang, B. C. Millar, and J. E. Moore. Antimicrobial resistance (amr). *British Journal of Biomedical Science*, 80:11387, 2023. doi:10.3389/bjbs.2023.11387.