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Multidrug-resistant *Escherichia coli*: Updated insights into resistance mechanisms, rapid diagnostics, and emerging control strategiesAsmaa S. Mansour[✉]

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ABSTRACT

Multidrug-resistant (MDR) *Escherichia coli* (*E. coli*) is a major global health threat, causing increased morbidity, mortality, and healthcare burden. It is a common cause of community- and hospital-acquired infections, with a strong ability to acquire and disseminate resistance genes *via* horizontal gene transfer and mutations. This review provides an overview of MDR *E. coli*, focusing on resistance mechanisms, diagnostic approaches, and control strategies. Key resistance mechanisms include production of extended-spectrum β -lactamases (ESBLs), carbapenemases, efflux pump overexpression, target site alterations, and reduced membrane permeability. Quorum sensing and biofilm formation further enhance bacterial survival and resistance. Diagnostic methods range from conventional antimicrobial susceptibility testing to advanced molecular and genomic techniques such as PCR and whole-genome sequencing. Emerging tools, including Fourier transform infrared spectroscopy, surface-enhanced Raman spectroscopy, MALDI-TOF MS, automated systems, and biosensors, offer rapid and accurate detection. Control strategies involve antimicrobial stewardship programs, alternative therapies such as natural compounds and QS inhibitors, and strict infection prevention measures. Addressing MDR *E. coli* requires a multidisciplinary approach integrating timely diagnosis, effective treatment, and robust infection control policies. A comprehensive literature search was conducted across major databases, and selected studies were qualitatively analyzed to summarize current knowledge and highlight emerging trends. Understanding these aspects is essential for limiting the spread of MDR *E. coli* and improving clinical outcomes globally.

KEYWORDS: Multidrug-resistant *Escherichia coli*; Antimicrobial resistance; Resistance mechanisms; Diagnostic techniques; Control approaches

1. Introduction

Escherichia coli (*E. coli*) is a Gram-negative, facultative anaerobic bacterium belonging to the Enterobacteriaceae family. It is a normal inhabitant of the intestinal tract of humans and animals; however, it can become pathogenic and cause a wide range of infections, particularly in the gastrointestinal and urinary systems[1,2]. Pathogenic *E. coli* strains are broadly classified into intestinal pathogenic *E. coli*, causing gastrointestinal infections, and extraintestinal pathogenic *E. coli*, responsible for urinary tract infections, sepsis, neonatal meningitis, and endometritis[3]. These strains harbor various virulence genes, including *eae*, *eagg*, *ipaH*, *stx-1*, *traT*, and *ompA*. In addition, they carry multiple antimicrobial resistance genes such as extended-spectrum beta-lactamases (ESBLs; *blaSHV*, *blaTEM*, and *blaCTX-M*), tetracycline resistance genes (*tetA* and *tetB*), and carbapenemase genes (*blaNDM*, *blaVIM*, and *blaIMP*)[4,5].

Since the discovery and widespread use of antibiotics in the early 1940s, their extensive application in human medicine, veterinary practice, and agriculture has accelerated the emergence of antimicrobial resistance (AMR)[6]. The World Health Organization (WHO) has identified AMR as one of the most serious public health threats of the century[7]. Consequently, multidrug-resistant (MDR)

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E. coli has become widely distributed in foods of animal origin, including meat, milk, dairy products, and poultry. Consumption of raw or undercooked products further facilitates their transmission to humans, while contaminated manure contributes to the spread of resistant bacteria into soil and water environments, posing significant public health risks[8,9]. MDR *E. coli* is of particular concern because its resistance to multiple antibiotics often results in treatment failure or limited therapeutic options, ultimately leading to elevated morbidity and mortality in both humans and animals[10].

The One Health concept highlights the interconnected transmission of antimicrobial-resistant bacteria among humans, animals, food, and the environment. The use of antimicrobial agents in food-producing animals for therapeutic purposes, disease prophylaxis, and growth promotion can select for resistant bacteria in the animal gut. These resistant organisms can subsequently spread through the food chain *via* meat and animal products, or through the application of manure and wastewater as fertilizers in agriculture, resulting in crop contamination. Humans acquire resistant bacteria either directly through the consumption of contaminated food or indirectly through environmental exposure. In addition, human-to-human transmission occurs in both community and healthcare settings, where resistant bacteria can spread *via* direct contact or contaminated surfaces, further amplifying the dissemination of AMR[11].

E. coli is frequently used as an indicator organism for AMR due to its prevalence in the intestinal tract and genomic plasticity, which enables the rapid acquisition of resistance genes[12]. Resistance may develop through chromosomal mutations or horizontal gene transfer mediated by mobile genetic elements such as plasmids, often associated with the dissemination of ESBL-producing strains[13,14]. Recent studies have reported increasing resistance to clinically important antibiotics, including carbapenems and colistin, alongside high resistance rates to agents such as penicillin, streptomycin, and neomycin among *E. coli* isolates[15,16].

Despite these observations, significant challenges remain in the early detection, accurate diagnosis, and effective control of MDR *E. coli*. This review aims to summarize recent advances in diagnostic approaches and control strategies, while highlighting current limitations and future perspectives for mitigating the public health impact of MDR *E. coli*.

2. Methods

A comprehensive literature search was performed to identify studies on MDR *E. coli*. The search was conducted across major electronic databases, including Scopus, Web of Science, and PubMed, covering publications up to 2026. Relevant keywords were used, such as “multidrug-resistant *E. coli*”, “antimicrobial resistance”, “resistance mechanisms”, “biofilm formation”, “diagnostic approaches”, “rapid detection methods”, “molecular typing”, and “control strategies”. Reference lists of selected articles were also manually screened to

identify additional relevant studies. Studies were screened according to predefined inclusion and exclusion criteria. Included studies were limited to those published in English and focusing on the resistance mechanisms, detection of diagnostic approaches, or control strategies of MDR *E. coli*. Duplicates, studies not directly related to MDR *E. coli*, and non-peer-reviewed articles were excluded. Appropriate data were extracted systematically. The collected material was then qualitatively combined to provide a comprehensive review of current knowledge and emerging trends in MDR *E. coli* research.

3. Resistance mechanisms of *E. coli*

As mentioned in Table 1, *E. coli* possesses multiple resistance mechanisms, including enzymatic inactivation of antibiotics. Among these, it produces ESBLs, which hydrolyze β -lactam antibiotics such as penicillins and cephalosporins. In addition, aminoglycoside-modifying enzymes inactivate aminoglycosides by altering their chemical structure, thereby preventing their binding to bacterial ribosomes. Furthermore, *E. coli* can produce carbapenemases, which confer resistance to carbapenems and significantly complicate treatment options[17,18].

E. coli also utilizes efflux pump systems, such as the AcrAB-ToIC complex, to actively expel antibiotics from the cell, thereby reducing their intracellular concentration. This mechanism confers resistance to multiple classes of antibiotics, including chloramphenicol and fluoroquinolones[19,20].

In addition, resistance can arise from mutations in antibiotic target sites. Fluoroquinolone resistance often results from mutations in DNA gyrase or topoisomerase IV, while trimethoprim resistance is associated with alterations in dihydrofolate reductase. These target modifications reduce antibiotic binding and confer bacterial resistance. In addition, modifications of lipopolysaccharides and outer membrane proteins decrease membrane permeability, further limiting antibiotic uptake[21].

Genetic mutations and horizontal gene transfer are key mechanisms driving AMR in *E. coli*. The organism acquires resistance genes through plasmids, bacteriophages, and other mobile genetic elements. This process contributes to the emergence of MDR, extensively drug-resistant, and pandrug-resistant strains. The resistance mechanisms in *E. coli* are multifactorial, enabling survival against a broad spectrum of antibiotics and posing significant challenges for treatment[22,23].

Quorum sensing (QS), also known as cell-density sensing, is a regulatory system that controls various physiological processes in bacterial cells. QS mechanisms are present in both Gram-positive and Gram-negative bacteria; however, the nature of signaling molecules differs between them. Bacteria synthesize signaling molecules known as autoinducers to facilitate intercellular communication[24]. QS plays a significant role in regulating virulence, antibiotic resistance, and biofilm formation in bacterial

strains[25].

Through QS mechanisms, bacterial cells communicate and coordinate various physiological processes, including those involved in horizontal gene transfer. This interaction facilitates the transfer of resistance plasmids between different bacterial species *via* conjugation (Figure 1). Consequently, previously susceptible bacteria may acquire resistance determinants. Ultimately, this contributes to the dissemination of AMR across diverse bacterial populations, increasing the prevalence of MDR organisms[26].

4. Comprehensive diagnostic strategies for MDR *E. coli*

4.1. Phenotypic detection

4.1.1. Antibiotic sensitivity test (Disk diffusion test)

Antimicrobial susceptibility testing is performed using the disk diffusion (Kirby-Bauer) method, a simple and widely used technique. A uniform bacterial lawn is inoculated onto the surface of agar plates, and antibiotic-impregnated discs are subsequently placed on

Table 1. Resistance mechanisms in multidrug-resistant (MDR) *Escherichia coli*.

Resistance mechanism	Main genes/factors	Antibiotic classes affected	Mechanism description	Detection methods	Reference
β -lactamase production	<i>bla</i> CTX-M, <i>bla</i> TEM, <i>bla</i> SHV	Penicillins and cephalosporins	Enzymatic hydrolysis of β -lactam ring of the antibiotic	Phenotypic ESBL tests, PCR, WGS	[17]
Carbapenemase production	<i>bla</i> KPC, <i>bla</i> NDM, <i>bla</i> OXA-48, <i>bla</i> VIM	Carbapenems	Enzymatic degradation of carbapenems	PCR, MALDI-TOF MS, WGS	[18]
Efflux pump overexpression	<i>acrAB-tolC</i> , <i>mdfA</i>	Multiple classes (tetracyclines, fluoroquinolones, etc.)	Active efflux of antibiotics from the bacterial cell	Gene expression assays, qPCR, WGS	[19,20]
Porin loss/modification	<i>ompF</i> , <i>ompC</i> alterations	β -lactams and carbapenems	Reduced antibiotic uptake due to decreased membrane permeability	WGS	[21]
Target site mutations	<i>gyrA</i> , <i>parC</i> , <i>rpoB</i>	Fluoroquinolones and rifampicin	Alteration of antibiotic binding sites	PCR, WGS	[21]
Plasmid-mediated resistance	R-plasmids with multiple genes	Multiple antibiotic classes	Horizontal gene transfer of resistance determinants	Plasmid profiling, WGS	[22,23]
Aminoglycoside-modifying enzymes	<i>aac</i> , <i>aad</i> , and <i>aph</i> genes	Aminoglycosides	Chemical modification of antibiotics	Phenotypic assays, PCR, WGS	[17]

ESBL: extended spectrum β -lactamase; PCR: polymerase chain reaction; qPCR: quantitative polymerase chain reaction; WGS: whole genome sequencing; MALDI-TOF MS: matrix laser desorption/ionization-time of flight mass spectrometry.

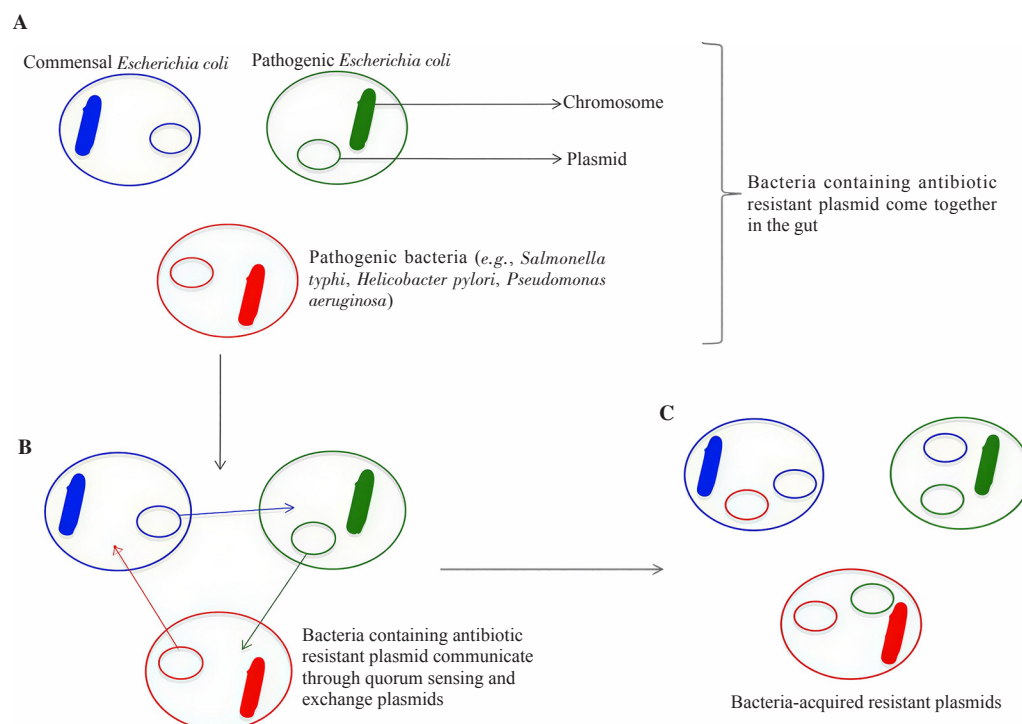


Figure 1. Horizontal transfer of antibiotic resistance plasmids among gut bacteria[26].

the agar. Following incubation, the diameters of the clear inhibition zones are measured. These zones reflect the effectiveness of each antibiotic against the tested organism. The results are interpreted according to standardized guidelines such as those established by Clinical and Laboratory Standards Institute or European Committee on Antimicrobial Susceptibility Testing, to classify the isolates as susceptible, intermediate, or resistant[27–29].

4.1.2. Double disc synergy test and modified double disc synergy test

The double disk synergy test is used for the phenotypic detection of ESBL production. In this method, a β -lactam antibiotic disc, such as ceftazidime or cefotaxime, is placed in proximity to a clavulanic acid-containing disc (*e.g.*, amoxicillin-clavulanate). Following incubation, a teardrop-shaped expansion of the inhibition zone toward the clavulanic acid disc indicates a synergistic effect, confirming the inactivation of β -lactamase by clavulanic acid. The presence of ESBL production is a strong indicator of multidrug resistance[30].

The modified double disk synergy test was performed using a similar procedure to the conventional double disk synergy test, with slight modifications in the arrangement and/or distance between antibiotic discs, and the use of multiple cephalosporins to improve the detection sensitivity of ESBL-producing isolates, particularly in isolates co-producing AmpC β -lactamases[29].

4.1.3. Broth microdilution (BMD)

The BMD method is a standardized phenotypic method used for antimicrobial susceptibility testing in *E. coli*. It is used to determine the minimum inhibitory concentration of antibiotics by exposing bacterial isolates to serial dilutions of antimicrobial agents in liquid media. This method provides precise and quantitative results, enabling accurate classification of isolates as susceptible, intermediate, or resistant according to the Clinical and Laboratory Standards Institute or European Committee on Antimicrobial Susceptibility Testing guidelines. Despite its high accuracy, BMD is labor-intensive and requires incubation time, which may limit its routine use in some clinical laboratories[28].

4.2. Molecular-based techniques

4.2.1. PCR techniques

These molecular techniques, including PCR, multiplex PCR (mPCR), and real-time PCR, are widely used for the amplification and detection of specific DNA sequences, enabling rapid and accurate identification of AMR genes[31,32]. Advantages and limitations of different molecular techniques are discussed in Table 2[33,34].

4.2.2. Microarrays

Microarray technology has emerged as a powerful molecular tool for the rapid detection and characterization of MDR *E. coli*. Microarrays consist of a solid surface onto which thousands of specific DNA probes are immobilized, allowing simultaneous hybridization with bacterial DNA. This enables the concurrent detection of multiple AMR genes in a single assay[35].

4.2.3. Isothermal amplification methods

Isothermal amplification methods represent a recent advancement over conventional PCR, as they enable nucleic acid amplification at a constant temperature without the need for thermocycling. Several types of isothermal amplification techniques have been developed, including nucleic acid sequence-based amplification and loop-mediated isothermal amplification[36]. Nucleic acid sequence-based amplification is primarily used for RNA amplification and requires strict RNA handling conditions. In loop-mediated isothermal amplification, amplification products can be detected visually through a color change or by fluorescence under a UV transilluminator[37].

4.2.4. Whole genome sequencing (WGS)

The WGS of bacteria is an advanced genomic approach that is increasingly accessible and can be applied in both human and animal research[38]. WGS is used for the comprehensive identification of microorganisms, as well as the detection of virulence factors and AMR mechanisms. In addition, WGS plays a crucial role in epidemiological surveillance and outbreak investigation, enabling precise tracking of transmission pathways and the spread of resistant strains. It is currently considered the reference standard for genomic surveillance of bacterial pathogens due to its comprehensive data output[39].

4.2.5. Restriction endonuclease analysis and restriction fragment length polymorphism

Restriction endonuclease analysis and restriction fragment length polymorphism are molecular techniques used to generate DNA fingerprints of bacterial strains. In these methods, restriction enzymes cleave genomic DNA at specific recognition sites, producing fragments of varying lengths. The resulting patterns are visualized typically using agarose gel electrophoresis. These techniques are used for the identification of bacterial strains and for tracking of MDR *E. coli* clones[40,41].

4.2.6. Pulse field gel electrophoresis

Pulse field gel electrophoresis is a molecular typing technique used for the separation of large DNA fragments generated by restriction enzyme digestion. Unlike conventional gel electrophoresis, pulse field gel electrophoresis applies an alternating electric field, allowing

the resolution of large DNA fragments, typically ranging from approximately 10 kb up to several megabases. In comparison, restriction endonuclease analysis generates smaller DNA fragments, usually in the range of 30-50 kb, which are separated using standard agarose gel electrophoresis[41]. Pulse field gel electrophoresis is widely used for epidemiological typing and tracking of clonal dissemination of MDR *E. coli*.

4.2.7. Random amplified polymorphic DNA

Random amplified polymorphic DNA is a PCR-based technique that uses a single short arbitrary primer to amplify random segments of genomic DNA. The amplified products are then separated by agarose gel electrophoresis and visualized using a UV transilluminator[33,42].

Table 2. Comparative overview of diagnostic methods for MDR *Escherichia coli*.

Method	Principle	Type	Advantages	Limitations	Turnaround time	Reference
Phenotypic AST (disc diffusion/ BMD)	Growth inhibition in media with antibiotics	Phenotypic	Simple, low-cost, standardized	Slow, 24-48 h, cannot detect resistance genes directly	Slow	[27–29]
PCR/qPCR	Amplification of specific resistance genes	Molecular	High sensitivity & specificity, rapid	Limited to known genes	Fast (2-4 h)	[31]
Multiplex PCR (mPCR)	Simultaneous amplification of multiple genes	Molecular	Multiple targets in one reaction	Complex optimization	Fast	[32]
Real-time PCR (TaqMan real-time PCR)	Real-time detection of target DNA, quantitative analysis of gene expression	Molecular	High sensitivity and specificity, accurate	High cost of equipment and reagents, skilled personnel, and susceptibility to contamination	Fast	[31]
Microarray	DNA-probe hybridization	Molecular	High-throughput detection of many genes	Expensive, known targets only, specialized equipment, and expertise	Moderate	[35]
Isothermal amplification LAMP/ NASBA	Constant temperature DNA amplification without thermocycling	Molecular	Rapid, simple, no thermal cycler, suitable for low-resource settings	Primer design complexity, risk of contamination, and non-specific amplification risk	Very fast (≤ 1 h)	[36,37]
Whole genome sequencing	Whole-genome DNA sequencing	Genomic	Highest resolution, detection of all genes, accurate	Costly, requires bioinformatics	Fast	[38,39]
REA/RFLP	Restriction enzyme DNA fragmentation patterns	Molecular typing	Simple, inexpensive	Low resolution, time-consuming, labor-intensive	Slow	[40,41]
PFGE	Restriction digestion + pulsed-field electrophoresis	Molecular typing	Good for outbreak tracking	Labor-intensive, low reproducibility	Slow	[41]
RAPD	Random PCR amplification patterns	Molecular typing	No prior sequence needed	Poor reproducibility, risk of contamination	Fast	[33,42]
FTIR spectroscopy	Infrared biochemical fingerprinting	Phenotypic	Rapid, label-free	Indirect, lower specificity	Fast	[43–45]
SERS	Raman signal enhancement fingerprinting	Phenotypic/ nano-biosensor	Ultra-sensitive, rapid	Cost and standardization issues	Very fast	[46]
Nanotechnology-based diagnosis	Nanomaterial-based detection	Technology-based	High sensitivity and specificity	Expensive, specialized equipment, sometimes toxic and non-biocompatible	Fast	[47–49]
MALDI-TOF MS	Protein spectral fingerprinting	Phenotypic (proteomic)	Very fast, accurate identification	Limited AMR detection	Very fast	[52–54]
Automated systems (VITEK 2/ Phoenix)	Biochemical + MIC-based automated analysis	Phenotypic	Rapid, standardized, high-throughput	Limited detection of novel resistance, instrument cost	Moderate (6-18 h)	[55]
Colorimetric biosensors (AuNPs)	Color change <i>via</i> target-bioreceptor interaction	Nano-biosensor	Simple, ultra-sensitive, cost-effective naked-eye detection	Qualitative	Very fast	[56,57]

AST: antimicrobial susceptibility testing; BMD: broth microdilution; LAMP: loop-mediated isothermal amplification; NASBA: nucleic acid sequence based amplification; REA: restriction endonuclease analysis; RFLP: restriction fragment length polymorphism; PFGE: pulse field gel electrophoresis; RAPD: random amplified polymorphic DNA; FTIR: Fourier transform infrared spectroscopy; SERS: surface-enhanced Raman spectroscopy; DNA: deoxyribonucleic acid; MIC: minimum inhibitory concentration; AMR: antimicrobial resistance.

4.3. Fourier transform infrared spectroscopy

Fourier transform infrared spectroscopy is a phenotypic and spectroscopic technique used to analyze the overall biochemical and chemical composition of bacterial cells. It provides a molecular “fingerprint” based on the vibrational transitions of cellular components such as proteins, lipids, and polysaccharides[43–45].

4.4. Surface-enhanced Raman spectroscopy

Surface-enhanced Raman spectroscopy is considered an advanced analytical technique that enables rapid and sensitive detection of bacterial pathogens based on their unique molecular fingerprints. By utilizing metallic nanostructures such as gold or silver nanoparticles, Raman signals are significantly amplified, allowing for precise characterization of cellular components. Surface-enhanced Raman spectroscopy can differentiate resistant from susceptible strains by variations in their spectral profiles, which reflect biochemical and structural changes associated with resistance mechanisms[46].

4.5. Nanotechnology-based diagnosis

Nanotechnology has attracted significant attention in recent years for the detection of various pathogens, including *E. coli*, as it helps overcome the limitations of culture-based and some molecular techniques[47–49]. The application of nanomaterials in bacterial diagnostics is mainly attributed to their large surface area-to-volume ratio, ease of surface functionalization, and unique optical

and physicochemical properties[50]. Another colorimetric approach for the detection of *E. coli* utilizes unmodified gold nanoparticles. This strategy is based on the differential electrostatic and structural properties between single-stranded DNA and double-stranded DNA[51].

4.6. Rapid diagnostic approaches

4.6.1. Matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI–TOF MS)

MALDI-TOF MS is a rapid and accurate technique for the identification of microorganisms based on protein profiling. Recently, it has also been explored for the detection of AMR in bacteria[52,53]. Although MALDI-TOF MS is a promising tool for AMR detection, further studies and standardization are still required before its routine implementation in clinical microbiology laboratories[54].

4.6.2. Automated systems

Automated systems such as VITEK 2 and BD Phoenix are widely used in clinical laboratories for the rapid identification of a wide range of microorganisms and antimicrobial susceptibility testing[55].

4.6.3. Colorimetric biosensors

Colorimetric biosensors are color-based detection approaches through qualitative detection of the target analyte, which is indicated by a visible color change that can be observed with the naked eye. These biosensors enable the detection of pathogens in biological fluids at very low concentrations[56]. In the presence of target

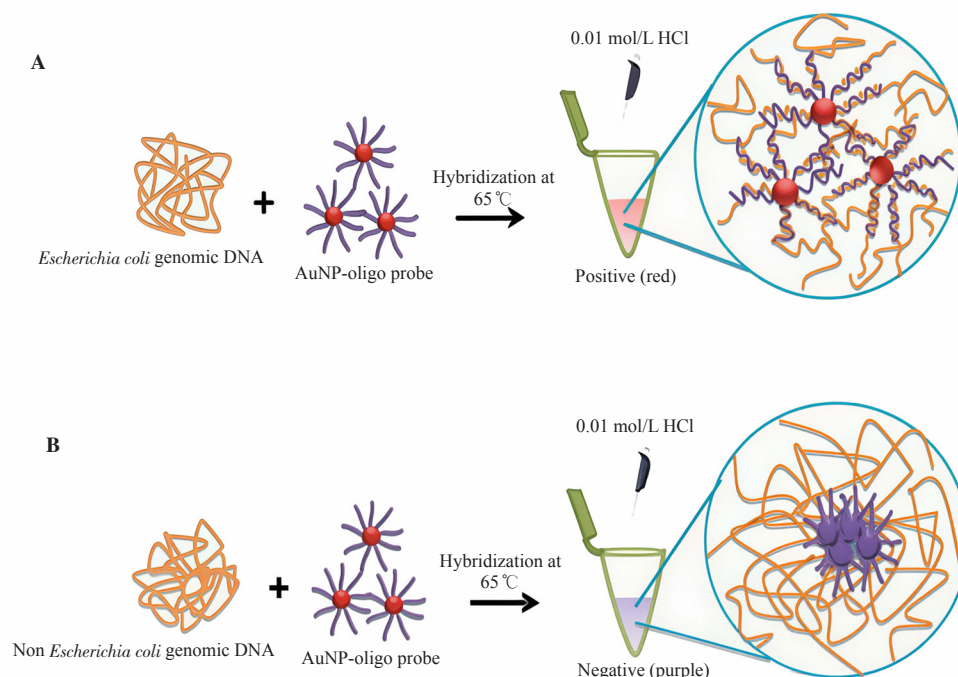


Figure 2. Schematic representation of working principle of AuNP-oligo probe assay[57]. AuNP: gold nanoparticles.

DNA, hybridization stabilizes the gold nanoparticles, preventing aggregation after acid addition and maintaining the red color (positive result). In the absence of target DNA, no hybridization occurs, leading to nanoparticle aggregation and a color change to purple (negative result), as shown in Figure 2[57].

Overall, diagnostic approaches for MDR *E. coli* vary significantly in terms of accuracy, cost, and turnaround time, which determines their suitability across different healthcare settings. In low-resource settings, diagnosis relies primarily on conventional phenotypic methods due to their affordability, simplicity, and minimal infrastructure requirements. Culture-based techniques followed by antimicrobial susceptibility testing, particularly disk diffusion, remain the most widely used approach as they provide reliable and standardized results, despite requiring longer incubation times.

In this context, phenotypic antimicrobial susceptibility testing—especially BMD for minimum inhibitory concentration determination—is considered the gold standard for defining resistance profiles according to the Clinical and Laboratory Standards Institute or European Committee on Antimicrobial Susceptibility Testing guidelines. Although disk diffusion is more commonly applied in routine laboratories due to its cost-effectiveness, it is less precise compared to BMD.

On the other hand, molecular and advanced diagnostic techniques, including PCR-based assays, WGS, MALDI-TOF MS, Fourier-transform infrared spectroscopy, and surface-enhanced Raman spectroscopy, offer rapid and highly accurate detection of bacteria and resistance mechanisms. These methods can provide results within minutes to a few hours; however, they are generally associated with high costs, specialized equipment, and the need for specialized expertise, which limits their routine use, particularly in resource-limited settings.

Therefore, a clear trade-off exists between speed and affordability, where rapid techniques offer timely and detailed insights but at high cost, while phenotypic methods remain the most practical and cost-effective option for routine diagnosis. Consequently, a combined or tiered diagnostic approach integrating phenotypic testing with selective molecular methods, where feasible, represents the most balanced strategy for effective MDR *E. coli* detection in diverse healthcare settings.

5. Integrated approaches for containment of MDR *E. coli*

5.1. Antibiotic stewardship programs

Antibiotic stewardship programs are essential strategies aimed at optimizing the use of antimicrobial agents to combat the emergence and spread of MDR *E. coli*. These programs focus on

the appropriate selection, dosing, duration, and route of antibiotic therapy[58]. In clinical settings, antibiotic stewardship programs rely on antimicrobial susceptibility testing to guide the selection of the most appropriate antibiotic. In veterinary and agricultural sectors, antibiotic stewardship programs emphasize the prudent use of antibiotics under veterinary supervision, along with reducing their use for growth promotion and prophylaxis[59].

5.2. Alternative and novel therapeutic approaches

5.2.1. Natural product-based and biologically derived therapeutic approaches

5.2.1.1. Bacteriocins

Bacteriocins are ribosomally synthesized antimicrobial peptides produced by various bacteria, including probiotic strains such as lactic acid bacteria. They exhibit antibacterial activity against closely related and pathogenic bacterial species[60,61].

5.2.1.2. Essential oils

Essential oils are volatile, lipophilic plant-derived extracts composed of bioactive secondary metabolites. These compounds contribute to plant defense against microbial pathogens and environmental stress. Several studies have reported their antibacterial activity against MDR *E. coli*[62–64].

5.2.1.3. Plant extracts

Medicinal plant extracts contain diverse phytochemicals, including phenolics, flavonoids, alkaloids, terpenoids, and tannins, which are responsible for their biological activity. These compounds have demonstrated antibacterial, anti-biofilm, and anti-virulence effects against MDR bacteria. For example, methanolic extracts of *Swietenia mahagoni* showed significant activity against *E. coli* (ATCC 35218)[65].

5.2.1.4. Endophytes

Endophytes are mutualistic symbiotic microorganisms that reside within plant tissues and produce bioactive secondary metabolites similar to those of their host plants. These metabolites exhibit antimicrobial potential through mechanisms such as inhibition of QS, biofilm formation, and essential cellular processes. Endophytes are classified into fungal and bacterial types and represent a promising source of novel antibacterial agents[10].

5.2.1.5. Lichens

Lichens are symbiotic associations between fungi and photosynthetic algae or cyanobacteria[66,67]. They produce a wide range of bioactive secondary metabolites with reported antibacterial and antifungal activities, contributing to their pharmacological potential[68,69].

5.2.1.6. Animal-associated natural products

Animal-derived compounds such as lysozyme, chitosan, and lactoferrin possess broad-spectrum antimicrobial activity. These molecules exert antibacterial effects through multiple mechanisms, including membrane disruption and inhibition of microbial growth[70].

5.2.1.7. Fungal metabolites

Fungi, particularly marine species, produce structurally diverse secondary metabolites, including alkaloids, terpenoids, peptides, steroids, and lactones. These compounds exhibit antimicrobial activity through mechanisms such as membrane disruption, oxidative stress induction, and inhibition of QS and biofilm formation[71,72].

5.2.1.8. Antimicrobial peptides

Antimicrobial peptides are ribosomally synthesized, gene-encoded peptides found in nearly all living organisms. In mammals, they are produced by epithelial cells and phagocytic cells as part of innate immunity[73]. They display a broad-spectrum of activities against MDR bacteria, primarily through membrane disruption, although some act *via* intracellular targets. In addition, they contribute to host defense by modulating immune responses and enhancing pathogen clearance[74,75].

5.2.1.9. Phage therapy

Phage therapy is a targeted antibacterial strategy that utilizes bacteriophages to lyse specific bacterial cells. It offers high specificity and low toxicity; however, concerns regarding horizontal gene transfer have led to increasing interest in bacteriophage-derived endolysins as safer alternatives[76,77].

5.2.1.10. QS inhibitors

QS inhibitors disrupt bacterial cell-cell communication systems, thereby reducing virulence, colonization, and biofilm formation[78]. In *E. coli*, QS is primarily mediated by autoinducer-2, which is produced *via* the activated methyl cycle by the LuxS enzyme, encoded by the *luxS* gene[79].

5.2.2. Nanotechnology-based approaches

Nanoparticles, such as silver, gold, and metal oxide nanoparticles, can be applied either alone or in combination with antibiotics to combat MDR *E. coli*. These nanomaterials exhibit potent antimicrobial activity through multiple mechanisms, including disruption of bacterial cell membrane, induction of oxidative stress, damage of proton efflux pumps, disruption of electron transport chain, prevention of biofilm formation, and DNA and protein damage[80,81].

Table 3. Control strategies for MDR *Escherichia coli*.

Control strategy	Main approach	Target/Mechanism	Advantages	Limitations	Relevance to MDR <i>Escherichia coli</i>	Reference
Antibiotic stewardship programs	Optimizing antibiotic use (selection, dose, and duration)	Reduces selective pressure and resistance emergence	Cost-effective, improves treatment outcomes	Requires multidisciplinary coordination and compliance	Essential for limiting spread of MDR strains	[58,59]
Natural products	Plant extracts, essential oils, lichens, and endophytes	Antibacterial, anti-biofilm, and anti-virulence	Biodegradable, diverse mechanisms	Variability and low standardization	Useful as alternative therapies	[10,62–64,65,66–68]
Antimicrobial peptides & bacteriocins	Ribosomal peptides from bacteria/hosts	Membrane disruption	Broad-spectrum, low resistance development	Stability and toxicity issues	Promising against MDR strains	[60,61,73–75]
Phage therapy & endolysins	Bacteriophage-mediated bacterial lysis	Targeted killing of bacteria	Highly specific, minimal microbiota disruption	Regulatory issues, potential gene transfer	Promising alternative for resistant strains	[76,77]
Quorum-sensing inhibition	Blocking bacterial communication (AI-2/LuxS system)	Inhibits virulence and biofilm formation	Reduces pathogenicity without killing bacteria	Mostly experimental	Important anti-biofilm strategy	[78,79]
Nanotechnology-based approaches	Nanoparticles (Ag, Au, metal oxides) with or without antibiotics	Membrane disruption, ROS generation, and drug delivery	Broad-spectrum, synergistic with antibiotics	Potential toxicity, cost, and limited clinical translation	Effective against biofilms and MDR strains	[80,81]
Theranostics & nanotheranostics	Combined diagnostic and therapeutic platforms	Detection + targeted treatment	Real-time monitoring and therapy	High cost, still experimental	Emerging precision approach	[82]
Bioinformatics & <i>in silico</i> approaches	Genome/protein analysis and drug design	Identification of targets and drug candidates	Fast and cost-effective	Requires experimental validation	Supports discovery of new therapeutics	[83]
Infection control & prevention	Hygiene, personal protective equipment, isolation, and disinfection	Prevents cross-transmission and hospital spread	Highly effective in healthcare settings	Inconsistent implementation in low-resource areas	Critical for nosocomial MDR <i>Escherichia coli</i> control	[84,85]

AI-2: autoinducer-2; Ag: silver; Au: gold; ROS: reactive oxygen species; MDR: multidrug-resistant.

5.3. Nanotheranostics

Theranostics is a combination of diagnostic and therapeutic functions integrated into a single platform, enabling simultaneous detection and treatment of pathogens using one agent[81]. Nanotheranostics is a nanotechnology-based form of theranostics that utilizes nanoparticles to combat antibiotic resistance and biofilm formation[82].

5.4. Bioinformatics strategies to limit antibiotic resistance

Bioinformatics is a field that integrates gene sequence analysis, structural alignment, and protein function prediction. This approach facilitates the discovery of new drugs that could serve as alternatives to conventional antibiotics, thereby addressing AMR[83].

5.5. Infection control & prevention

In hospitals, strict personal hygiene, the use of personal protective equipment, proper sterilization of medical instruments, and environmental disinfection are crucial to prevent cross-transmission. These measures should be accompanied by the isolation of infected patients and ensuring food and water safety to avoid fecal-oral transmission[84]. In the veterinary sector, control measures include strict hygiene practices, disinfection of equipment and housing, proper treatment of animal manure, and regular surveillance of AMR in livestock, which support early detection and control of MDR strains[85]. Control strategies are summarized in Table 3.

6. Challenges in managing MDR *E. coli* and future perspectives

Efficient diagnosis and control of MDR *E. coli* face significant challenges in both clinical and veterinary settings. One of the primary diagnostic limitations is the reliance on culture-based methods, which are time-consuming and may delay the initiation of appropriate therapy. Although molecular techniques enable rapid and sensitive detection of resistance determinants, their use is often constrained by high cost, the need for specialized equipment, and technical expertise, particularly in resource-limited settings. In addition, the extensive genetic diversity of resistance mechanisms in *E. coli* complicates accurate detection, as novel or uncommon resistance genes may be missed by targeted assays[86–88].

From a clinical perspective, distinguishing between colonization and active infection represents another major challenge, potentially leading to inappropriate antibiotic use. Moreover, biofilm formation by *E. coli* can further hinder both accurate detection and reliable antimicrobial susceptibility testing[89].

Regarding control strategies, the rapid emergence and dissemination of MDR *E. coli* significantly limit available therapeutic options. The overuse and misuse of antibiotics in human, animal, and agricultural sectors continue to drive the development of resistance. Although infection control measures are effective, their implementation is often inconsistent due to limitations in healthcare infrastructure, inadequate surveillance systems, and insufficient awareness. Furthermore, the global spread of high-risk clones and mobile genetic elements, such as plasmids carrying resistance genes, further complicates containment efforts[90].

These challenges highlight the urgent need for the development of rapid, cost-effective diagnostic tools, alongside the implementation of robust antimicrobial stewardship programs and coordinated global surveillance strategies to effectively combat MDR *E. coli*[91].

7. Conclusion

In summary, MDR *E. coli* remains a significant global health threat, particularly in low-resource settings, driven by widespread antibiotic misuse, rapid dissemination of resistance genes, and biofilm-associated persistence. The use of advanced diagnostic technologies is limited by cost, accessibility, complexity, and the genetic diversity in resistance mechanisms. Addressing this challenge requires a One Health approach integrating improved surveillance, antimicrobial stewardship, and infection control. Future efforts should highlight on developing rapid, affordable diagnostics and exploring novel therapies, including anti-virulence strategies, nanotechnology-based systems, and other non-traditional interventions, to better manage and control MDR *E. coli*.

Conflict of interest statement

The author declares that there is no conflict of interest.

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During the preparation of this work, the author used ChatGPT to paraphrase a few sections of the manuscript, without involvement in data collection, analysis, or any other scientific work. The author reviewed and edited the content and takes full responsibility for the publication.

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