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Review Article

A Review on Escherichia coli Vaccine Development: Current Progress and Future Prospects

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Abstract

Escherichia coli (*E. coli*) is a diverse bacterium commonly found in the intestinal tract of humans and animals. While many strains are harmless, pathogenic variants such as enterotoxigenic (ETEC), enterohemorrhagic (EHEC), and avian pathogenic (APEC) strains cause significant health problems in humans and livestock. In Pakistan, *E. coli* infections are especially problematic in the poultry and dairy industries, where they cause economic losses through mortality, decreased productivity, and increasing antibiotic resistance. The overuse of antibiotics has further intensified the problem, making vaccine development an important alternative preventive strategy. This review summarizes current approaches to *E. coli* vaccine development, including inactivated vaccines, attenuated vaccines, recombinant protein-based vaccines, DNA vaccines, and autogenous farm-specific vaccines. Each approach is considered in terms of its mechanism, potential advantages, limitations, and applicability to different *E. coli* pathotypes. Particular attention is given to antigenic diversity, mucosal immunity, antimicrobial resistance, and the need for vaccines adapted to strains circulating in Pakistan. The review also discusses recent international progress, research gaps, infrastructure limitations, and future priorities. Developing effective and locally relevant *E. coli* vaccines could reduce antibiotic reliance, improve animal and public health, strengthen farm biosecurity, and support microbiological research and vaccine innovation in Pakistan. The review emphasizes that vaccine performance varies with pathogen type, antigen selection, delivery route, and the ability to induce durable protective immunity.

Keywords

Escherichia Coli, Vaccine Development, Antimicrobial Resistance. APEC, ETEC, Recombinant Vaccines, Pakistan

1. Introduction

Escherichia coli (*E. coli*) is one of the most extensively studied bacterial species and was first identified by Theodor Escherich in 1885. It is a Gram-negative, rod-shaped, facultative anaerobic bacterium that commonly inhabits the gastrointestinal tract of humans and warm-blooded animals, where it plays an important role in maintaining intestinal homeostasis [1]. Most *E. coli* strains are harmless commensals; however, certain strains have acquired virulence factors through horizontal gene transfer, enabling them to cause a wide range of intestinal and extra-intestinal diseases.

Pathogenic *E. coli* strains are responsible for serious infections including diarrhea,

hemorrhagic colitis, urinary tract infections (UTIs), septicemia, and meningitis. Based on their virulence mechanisms and clinical manifestations, pathogenic *E. coli* are classified

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into several pathotypes such as enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), enterohemorrhagic *E. coli* (EHEC), enteroinvasive *E. coli* (EIEC), and avian pathogenic *E. coli* (APEC). These strains produce toxins, adhesins, invasins, and other virulence factors that enable them to colonize host tissues and evade immune responses.

In the livestock and poultry industries, *E. coli* infections represent a major economic and health concern. Avian pathogenic *E. coli* (APEC) is a leading cause of colibacillosis in poultry, resulting in respiratory infections, septicemia, reduced egg production, and high mortality rates.

Similarly, enterotoxigenic *E. coli* (ETEC) is a major cause of neonatal diarrhea in calves and piglets, leading to dehydration, growth retardation, and significant economic losses [13]. In developing countries such as Pakistan, where poultry farming plays a vital role in food security and the national economy, frequent *E. coli* outbreaks severely affect productivity and profitability [2].

Moreover, the widespread and often inappropriate use of antibiotics in both human and veterinary medicine has contributed to the emergence of multidrug-resistant *E. coli* strains. These resistant strains pose a serious threat to public health by limiting available treatment options and increasing morbidity and mortality rates [3]. The rapid spread of antimicrobial resistance has emphasized the urgent need for alternative preventive strategies.

Consequently, global research efforts have increasingly focused on vaccine development as a sustainable and effective approach to control *E. coli* infections. Vaccination offers long-term protection, reduces reliance on antibiotics, and helps limit the spread of resistant strains. Understanding the pathogenic mechanisms, virulence factors, and epidemiology of *E. coli* is therefore essential for the development of effective vaccines and control strategies. Despite extensive research, vaccine development remains challenging due to antigenic diversity and differences between intestinal and systemic infections.

Effective vaccines must not only target virulence factors but also stimulate appropriate immune pathways, particularly mucosal immunity.

As a narrative review, literature for this article was collected from databases including PubMed and Google Scholar, focusing mainly on studies published from 2020 onward to ensure updated and relevant information.

2. Need for Vaccine Development

2.1. Rising Antibiotic Resistance

Recent studies in Pakistan have reported a dramatic increase in resistance of *E. coli* isolates against commonly used antibiotics including fluoroquinolones, cephalosporins, tetracyclines, and trimethoprim-sulfamethoxazole [4, 5]. The presence of ESBL (extended-spectrum beta-lactamase) and carbapenemase genes (blaNDM-5, blaOXA-181) has made several clinical isolates multidrug-resistant, causing therapeutic failures [6]. This increasing resistance highlights a shift from treatment-based approaches to preventive immunization strategies, making vaccines a critical tool in antimicrobial stewardship.

2.2. Public Health Significance

In humans, pathogenic *E. coli* is responsible for diarrheal outbreaks, urinary tract infections, sepsis, and foodborne illnesses. These infections are more severe and costlier to treat due to limited antibiotic options [7].

2.3. Agricultural Losses

In poultry, APEC causes colibacillosis resulting in high mortality, poor growth performance, and condemnation of carcasses at processing plants. In dairy cattle, *E. coli* mastitis is one of the most significant diseases causing reduction in milk yield and quality [8].

2.4. Economic Impact

Livestock and poultry farmers face direct economic losses due to decreased productivity, increased treatment costs, and culling of infected animals. At a national level, this leads to reduced food supply and lower export potential.

2.5. Local Strain Variability

Studies show that Pakistani *E. coli* isolates have unique serotypes and virulence gene profiles compared to international reference strains [2]. Hence, locally developed vaccines are crucial for effective protection.

2.6. One Health Perspective

Antibiotic-resistant *E. coli* is shed into the environment through animal waste, contaminating soil and water and contributing to human infections. Vaccination reduces bacterial shedding and improves farm biosecurity [9].

2.7. Sustainable Solution

Vaccines are cost-effective, environmentally safe, and reduce the need for antibiotics, thereby slowing the development of antimicrobial resistance.

Table 1. *Factors influencing the need for E. coli vaccination.*

Factors	Impact	Role of vaccine
Antibiotic Resistance	Treatment failure	Prevent infection
Public Health Burden	Increase mortality	Reduce disease spread
Agricultural Loss	Economic damage	Improve productivity
Environmental spread	One Health risk	Reduce shedding

3. Types of *E. coli* Vaccines

3.1. Inactivated (Killed) Vaccines

These are made by chemically or physically killing pathogenic strains while retaining antigenicity. They are safe, stable, and relatively easy to prepare, but often induce weaker immune responses compared to live vaccines. Booster doses are usually required.

3.2. Attenuated (Live Weakened) Vaccines

These involve genetically modifying or passaging bacteria so that they lose virulence but still stimulate immunity. Attenuated vaccines provide stronger and longer-lasting immunity, mimicking natural infection. However, safety concerns exist, especially in immunocompromised hosts.

3.3. Recombinant Protein-Based Vaccines

Specific *E. coli* proteins, such as outer membrane proteins (OMPs), toxins, or adhesins, are expressed using recombinant DNA technology. These vaccines are highly specific and safe, but their production requires advanced microbiology facilities and adjuvants to enhance efficacy. Recombinant vaccines have shown relatively better success against APEC compared to EHEC because APEC mainly causes systemic infections where circulating antibodies can easily reach bacterial targets.

3.4. DNA Vaccines

Plasmids carrying genes encoding *E. coli* antigens are delivered to host cells, where the antigen is expressed and elicits immunity. DNA vaccines are stable, safe, and easy to design, but their use in veterinary practice is still limited due to regulatory concerns.

3.5. Autogenous (Farm-Specific) Vaccines

In regions like Pakistan, autogenous vaccines prepared from local *E. coli* isolates can be highly effective. These are tailored to the exact strains circulating on farms, providing targeted protection [10].

Table 2. *Comparison of E. coli vaccine types.*

Vaccines types	Safety	Immunity	Limitation
Inactivated	High	Moderate	Weak response
Live	Moderate	Strong	Safety risk
Recombinant	High	Targeted	Expensive
DNA	High	Experimental	Limited use
Autogenous	High	Localized	Not universal

3.6. Why Some Vaccines Fail

Despite significant progress in vaccine development, many *E. coli* vaccines do not provide complete protection. One major reason is the lack of mucosal immunity, which is essential for protection against intestinal infections. Most vaccines are administered via injection and mainly stimulate systemic immunity (IgG antibodies), but pathogens like ETEC and EHEC

colonize the intestinal lining where secretory IgA (sIgA) plays a key protective role. Without strong mucosal immunity, bacteria can still attach and multiply in the gut. [12] Another important factor is antigenic variation. *E. coli* strains show high diversity in surface antigens such as O-antigens, fimbriae, and toxins. This means a vaccine developed against one strain may not be effective against others circulating in different regions, especially in countries like Pakistan where local strains differ genetically [2] Additionally, poor antigen selection can reduce vaccine effectiveness. Some vaccines target non-essential or less conserved proteins, which do not provide strong or long-lasting protection. Effective vaccines should target conserved virulence factors such as outer membrane proteins or adhesins that are common across multiple strains [6] These challenges explain why vaccines against systemic infections like APEC tend to perform better than those targeting intestinal infections, as systemic immunity is easier to achieve compared to mucosal immunity.

3.7. Immunological Mechanism of *E. coli* Vaccines

The effectiveness of *E. coli* vaccines depends on their ability to activate both humoral and cellular immune responses. Firstly, humoral immunity (B-cell response) plays a central role. Vaccination stimulates B-cells to produce antibodies such as IgG and IgA. These antibodies can neutralize bacterial toxins (e.g., enterotoxins in ETEC) and block adhesion of bacteria to host cells, preventing colonization [11] Secondly, mucosal immunity is particularly important for enteric infections. Secretory IgA (sIgA) is produced at mucosal surfaces and acts as the first line of defense by preventing bacterial attachment to intestinal epithelial cells. However, many current vaccines fail to effectively stimulate this response, which limits their protective ability [9] Thirdly, cell-mediated immunity (T-cell response) supports long-term protection. Helper T-cells (Th1 and Th2) activate macrophages and enhance antibody production, while memory T-cells ensure a faster response upon re-exposure to the pathogen [8] Finally, the development of immune memory is essential for long-lasting protection. A successful vaccine ensures that the immune system can quickly recognize and eliminate *E. coli* during future infections. Overall, an ideal *E. coli* vaccine should stimulate a balanced immune response, including strong mucosal immunity, which remains a major challenge in current vaccine strategies.

4. Global Progress and Pakistani Context

4.1. International Advances

Globally, several vaccine candidates have been tested, including the ExPEC9V bioconjugate vaccine developed by Janssen and Sanofi for prevention of invasive extraintestinal pathogenic *E. coli* disease. In February 2025, an independent review of the Phase 3 E. mbrace study found that the vaccine was not sufficiently efficacious in preventing invasive *E. coli* disease, although no safety signals were identified; the study was discontinued. These findings highlight the difficulty of achieving effective protection against extraintestinal *E. coli* infections.

4.2. Emerging Technologies

Recombinant subunit vaccines targeting conserved outer membrane proteins and fimbrial adhesins are showing promising results in experimental trials. DNA and mRNA-based vaccines are also being investigated for their ability to induce long-lasting immunity. mRNA technology is considered a promising future strategy because it allows rapid vaccine design and modification according to emerging strains.

4.3. Pakistani Context

Research in Pakistan remains limited, with most studies focusing on antimicrobial resistance surveillance rather than vaccine development [2]. However, promising work has been done at UVAS Lahore, where a monovalent *E. coli* (aggR) mastitis vaccine was developed and successfully tested in cattle, showing good immunogenic response [8].

4.4. Research Gaps

There is a need for large-scale field trials, genomic characterization of local strains, and public-private partnerships to support commercial production of *E. coli* vaccines in Pakistan. Pakistan lacks advanced vaccine production facilities and relies heavily on imported technologies, limiting local innovation.

5. Challenges and Future Directions

5.1. Genetic Diversity of *E. coli*

Multiple pathotypes (APEC, ETEC, EHEC, ExPEC) and numerous serotypes make it difficult to design a single universal vaccine.

5.2. Limited Research Infrastructure

Pakistan lacks advanced molecular biology labs and facilities for recombinant vaccine development and production at scale.

5.3. Cost and Accessibility

Commercial vaccines are often expensive and unaffordable for small-scale farmers. Government subsidies and awareness programs are needed to ensure widespread adoption.

5.4. Need for Multivalent Vaccines

Vaccines targeting multiple virulence factors and serotypes are essential for broad-spectrum protection in field conditions.

5.5. Regulatory and Logistical Barriers

Proper licensing, quality control, and cold chain management are needed to ensure vaccine safety and efficacy.

5.6. Future Research Priorities

Focus should be placed on recombinant protein-based vaccines using local isolates, development of adjuvants that boost mucosal immunity, and integration of vaccination programs with antimicrobial stewardship under a One Health framework [6, 9].

6. Conclusion

E. coli remains a significant health and economic challenge in Pakistan. While global research has made progress in vaccine development, Pakistan still lags behind. Developing vaccines from indigenous isolates can reduce antibiotic dependency, safeguard livestock and human health, and promote scientific advancement. For Pakistan, investment in vaccine research is not only a medical necessity but also an agricultural and economic priority. Major barriers still exist due to antigenic diversity, limited mucosal immunity, and infrastructural limitations.

Abbreviations

APEC	Avian Pathogenic Escherichia coli
EHEC	Enterohemorrhagic Escherichia coli
EPEC	Enteropathogenic Escherichia coli
ETEC	Enterotoxigenic Escherichia coli
EIEC	Enteroinvasive Escherichia coli
EXPEC	Extraintestinal Pathogenic Escherichia coli
ESBL	Extended-spectrum beta-lactamase
IgA	Immunoglobulin A
IgG	Immunoglobulin G
OMP	Outer Membrane Protein
sIgA	Secretory immunoglobulin A
UTI	Urinary Tract Infection

Author Contributions

Tayyaba Fatima: Conceptualization, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing

Conflicts of Interest

The author declares no conflicts of interest.

References

[1] Kaper, J. B., Nataro, J. P., & Mobley, H. L. T. (2004). Pathogenic Escherichia coli. Nature Reviews Microbiology, 2, 123–140. https://doi.org/10.1038/nrmicro818

[2] Rehman, A., Zahra, R., & Akhtar, M. (2021). Multidrug resistance and pathogenicity of avian *E. coli* isolates in Pakistan. Journal of Animal and Plant Sciences, 31(3), 772–780.

[3] Ali, T., ur Rahman, S., Zhang, L., Shahid, M., & Han, D. (2019). Characteristics and antibiotic resistance of *E. coli* from dairy cows in Pakistan. Frontiers in Microbiology, 10, 1377.

[4] Shaheen, T., Tariq, A., & Ali, S. (2019). Antimicrobial resistance patterns of *E. coli* isolated from poultry in Pakistan. Pakistan Journal of Zoology, 51(5), 1759–1766.

[5] Ahmad, M., et al. (2022). Prevalence of ESBL-producing *E. coli* in poultry and dairy farms in Pakistan. Microbial Drug Resistance, 28(3), 215–225.

[6] Sattar, F., Hu, X., Saxena, A., Mou, K., Shen, H., Ali, H., Ghauri, M. A., Sarwar, Y., Ali, A., & Li, G. (2024). Analyzing antibiotic resistance in bacteria from wastewater in Pakistan using whole-genome sequencing. Antibiotics, 13(10), 937. https://doi.org/10.3390/antibiotics13100937

[7] Khan, M. A., et al. (2021). Trends in multidrug-resistant *E. coli* from clinical samples in Punjab, Pakistan. BMC Microbiology, 21(1), 312.

[8] Akhtar, M., et al. (2022). Development and evaluation of *E. coli* (aggR) vaccine against mastitis in cattle. Pakistan Veterinary Journal, 42(1), 33–39.

[9] Yaseen, T., et al. (2023). One Health approach to controlling antimicrobial resistance in Pakistan: Focus on livestock sector. Frontiers in Veterinary Science, 10, 11234.

[10] Ahmad, A., Hussain, I., Akhtar, M., & Muhammad, K. (2020). Development of farm-specific autogenous vaccines for controlling colibacillosis in poultry. Pakistan Veterinary Journal, 40(2), 215–220.

[11] Garcia, C. Y., Seo, H., Sack, D. A., & Zhang, W. (2022). Intradermally administered enterotoxigenic Escherichia coli vaccine candidate MecVax induces functional serum immunoglobulin G antibodies against seven adhesins and both toxins. Applied and Environmental Microbiology, 88(4), e02139-21. https://doi.org/10.1128/AEM.02139-21

[12] Johnson & Johnson. (2025, February 13). Johnson & Johnson statement on Phase 3 E. mbrace study. https://www.jnj.com/media-center/press-releases/johnson-johnson-statement-on-phase-3-e-mbrace-study

[13] Kabir, S. M. L. (2010). Avian colibacillosis and salmonellosis: A closer look at epidemiology, pathogenesis, diagnosis, control and public health concerns. International Journal of Environmental Research and Public Health, 7(1), 89–114. https://doi.org/10.3390/ijerph7010089