

Diarrheagenic *Escherichia Coli* and probiotic activity against foodborne pathogens: A brief review

Abstract

Diarrheagenic *Escherichia coli* (DEC) represents the most common bacterial pathogen worldwide and is often involved in intestinal illnesses caused by food borne pathogens. DEC generally cause auto limited watery diarrhea that in some cases can progress to more severe disease, what is related to a range of virulence factors. Probiotic bacteria naturally live in microflora and confer health benefits to the host. *Lactobacillus* and *Bifidobacterium* species are the most commonly used as probiotics in research and studies highlighted probiotic activity against DEC and other food borne pathogens by these strains. Studies show that probiotic strains have antimicrobial properties, inhibiting virulence *in vitro* and *in vivo* and providing immunomodulation. However, the role of probiotics against pathogenic *E. coli* is still little known and further studies are needed to understand probiotic mechanisms against DEC.

Keywords: Diarrheagenic *Escherichia coli*, Food borne pathogens, probiotic activity, *Lactobacillus*, *Bifidobacterium*

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Abbreviations: DEC, diarrheagenic *Escherichia coli*; ETEC, enterotoxigenic *E. coli*; EHEC, Enterohemorrhagic *E. coli*; STEC, shiga-toxin *E. coli*; EPEC, Enteropathogenic *E. coli*; EIEC, Enteroinvasive *E. coli*; EAEC, Enteroaggregative *E. coli*; DAEC, Diffusely adherent *E. coli*

Introduction

Foodborne pathogens cause several diseases, most associated with intestinal symptoms. Bacterial enteropathogens species are highlighted as the cause of several gastrointestinal illnesses, which includes pathogenic *Escherichia coli*. Diarrheagenic *Escherichia coli* (DEC) represents the most common bacterial pathogen worldwide.¹

E. coli strains are naturally commensal bacteria that live in intestinal tract of humans and other mammals. Some strains are pathogenic and can cause disease, especially intestinal.² Diarrheagenic *E. coli* strains are classified into six categories, based in clinical syndromes, symptoms, epidemiology, O:H serotypes, virulence factors and interaction with *in vitro* cultivated cells.³ All enteropathogenic *E. coli* types cause generally watery diarrhea as a common symptom. Most episodes of intestinal dysfunction are auto limited and solved in a few days, but some rare cases can progress to more severe disease.^{2,3}

Probiotics are live nonpathogenic microorganisms that confer health benefits.⁴ Some bacterial probiotic strains provide protection from pathogens to their human hosts, naturally living in the urogenital and gastrointestinal microflora and being usually found in fermented food, like dairy products.^{5,6}

Diarrheagenic *Escherichia coli*

Enterotoxigenic *E. coli* (ETEC) strains are enterotoxic (produce heat-stable and heat-labile toxins) and non-invasive of the small intestine, highly associated to traveler's disease.⁷ Enterohemorrhagic *E. coli* (EHEC) is a common as a food or water-borne pathogen in developing countries. High importance is given to O157:H7 serotype, isolated from stool samples diarrhea outbreaks caused by *E. coli*. This serotype is related to Shiga-toxin production (Shiga-toxin *E. coli* - STEC) and destruction of epithelium, which

are associated with the development of severe complications, such hemorrhagic colitis and hemolytic uremic syndrome.⁸ Despite being close related to EHEC, enteropathogenic *E. coli* (EPEC) strains are non-toxin-producing bacteria associated with acute and protracted diarrhea in children in developing countries.^{3,9} Enteroinvasive *E. coli* (EIEC) strains are highly invasive and non-producing toxins. The pathogenic mechanism is similar in many aspects to the syndrome caused by *Shigella* causing severe damage in the intestinal wall by cell destruction.¹⁰ Enteroaggregative *E. coli* (EAEC) is defined as *E. coli* that do not produce the heat-stable or heat-labile toxins of ETEC and manifest a characteristic aggregative ('stacked brick') pattern of adherence to HEp2-cells in culture. This pathotype is related to persistent diarrhea in children.^{1,11} Diffusely adherent *E. coli* (DAEC) refers to any HEp-2-adherent *E. coli* strain that form diffuse pattern of adhesion. Its role in diarrhea development is not clearly known.²

Probiotic activity against DEC and Other Foodborne Pathogens

Lactobacillus and *Bifidobacterium* species are the most commonly used as probiotics in research and some of them are addressed below. Studies highlighted these probiotic strains activities against DEC and other foodborne pathogens, such as reduction of biofilm development, inhibition of adhesion and injury of *in vitro* cultivated cells, preventing diarrhea on *in vivo* models and immunomodulation.

L. acidophilus was capable to reduce *E. coli* O157:H7 (EHEC) and *E. coli* O127:H6 (EPEC) adhesion to T84 cells.⁹ and *Listeria monocytogenes* biofilm formation, which was susceptible to probiotic cultures.¹² Compared to antibiotic use, *L. acidophilus* showed great inhibition of *Campylobacter jejuni*, *E. coli* O157 and *S. typhimurium* strains. Furthermore, *in vivo*, *L. acidophilus* reduced or prevented diarrhea in albino rats co-infected with *Campylobacter jejuni*.¹³ Synergistically to *L. plantarum*, *L. acidophilus* showed better dose-dependent antimicrobial activity against multidrug resistant EAEC when compared to monostrain condition, also being efficient to decrease EAEC counts in infected mice feces.¹⁴ *L. plantarum* showed antimicrobial activity against several enteropathogenic bacteria, including *Listeria monocytogenes*, *Shigella sonnei*, *Salmonella*

Typhimurium, *Staphylococcus aureus* and *E. coli* O157:H7. Also, *L. plantarum* promoted reduction of cell adhesion by *E. coli* O157:H7, *S. aureus* and *Salmonella* in Caco-2 cells and increased expression of an anti-inflammatory cytokine IL-10 and decreased expression of proinflammatory cytokines IL-6, IL-8, and TNF- α by the cells when co-cultivated with *Salmonella*.¹⁵ Otherwise, in a previous study *L. casei* and *L. plantarum* showed no effect on binding or invasion of *E. coli* O157:H7 in Caco-2 cells, meanwhile *L. rhamnosus* showed outstanding potential for adhering to the cells and inhibiting *E. coli* invasion.¹⁶ As observed with *L. acidophilus*, *L. rhamnosus* also promoted a dose-dependent reduction in the adhesion of *E. coli* O157:H7 to HEp-2 and T84 cells, decreasing foci of cytoskeletal rearrangement numbers, which are referred to attaching and effacing lesions⁹ and *Listeria monocytogenes* biofilm formation.¹² Similar results were found in another study, where polarized MDCK-I and T84 cells pretreated with *L. rhamnosus* reduced morphological changes and decreased attaching-effacing lesions induced by *E. coli* O157:H7 infection.¹⁷ In addition, *L. casei* promotes specific immune responses against *E. coli* O157:H7 cytotoxins and enhances the elimination of bacteria from the intestinal tract in infected rabbits.¹⁸ *L. casei* can also be a vector of heterologous EPEC antigens, stimulating the immune system to produce antibodies that inhibit EPEC adherence to HEp-2 cells.¹⁹

There are fewer studies about *Bifidobacterium* spp. probiotic properties against bacterial enteropathogens when compared to lactobacilli and this involves a range of multispecies evaluation. *B. breve* is capable to protect murine intestinal infection caused by *E. coli* O157:H7. The strain modifies pH due to production of high levels of acetic acid and inhibits Shiga-toxin production by STEC growth *in vitro*.²⁰ *B. lactis* and *B. longum* showed antimicrobial activity against *Shigella sonnei* and have protective properties against uropathogenic *E. coli*.²¹ A *B. lactis* strain provided protection to *Salmonella* infection in mice, increasing survival rate and reducing bacterial translocation to spleen and liver.²² *B. animalis* and *B. lactis* also promote immunomodulation of mucosa, increasing the number of IgA+ cells.²³ Increasing in cytokine production and natural killer cells activity can be provided by *B. animalis* and lactobacilli. This property is related to yoghurt consumption, which is a font of multispecies probiotics.⁶

Conclusion

Probiotic bacteria have potential therapeutic effect and can be used as an alternative treatment in gastrointestinal illnesses. Different strains of the most studied probiotic species promote activity against a range of enteropathogenic bacteria, inhibiting growth, virulence *in vitro* and *in vivo*, competing and providing immunological response, especially when they act synergistically. The role of probiotics against pathogenic *E. coli* is still little known. Thus, further studies are needed to understand the role of probiotics activity against DEC.

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Conflicts of interest

The authors declare there is no conflict of interest.

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