Role of Probiotics in Enteric Disease Management And Their Antivirulence Properties: A Review

Hasnain Farooq¹, Kaleem Ullah¹, Zunair Akma¹, Amir Hussain Shahzad¹, Affifa Tajamma¹*, Aisha Waheed Qureshi¹

¹Department of Biology, Lahore Garrison University, Lahore, Pakistan
*affifa.tajammal@lgu.edu.pk

Abstract:
Probiotics have been the core area of study since last few decades due to their immense beneficial effects on human health. They are widely incorporated as a verity of products in food industry. Prebiotics are the commonly used fibers and when used in combination with probiotics are called as synbiotics, thus enhancing the probiotic activity. Several in vitro and in vivo studies have revealed the application of these microbiota management tool for the prevention and cure of diseases. Diarrhea prevention, atopiceczema, dental care, cancer therapy and treatment of bowel syndrome are the various health benefits provided by probiotic activity. These wonderful microorganisms have the enzymatic activity of breakdowning the food macromolecules, secretion of anti microbial substances, anti-carcinogenicability, enhancing immune system, improved ability in producing short-chain fatty acid, anti atherogenicability, allergen regulation, anti-virulence activity, treatment of urinary tract infections and many more. In the light of this remarkable ongoing trend and the scientific evidence obtained on these microbiota, it is the need of hour to do further research on dose and optimal probiotic for specific diseases. This narrative review present the current documentation on enteric disease management stratagies and anti-virulence studies focusing on quantum sensing inhibition, anti-toxin effects and anti-invasion effects.

Keywords: human health issues; probiotic activity; disease management; Antivirulence activity; next generation probiotics

Introduction:
Infectious disorders are the main cause of about 18 million deaths every year globally in accordance with the reports of World health organization (WHO). Antibiotic resistance is the major risk factor for the health care sector¹. Nonpathogenic bacterial associations to their food sources formerly known as prebiotics, probiotics and symbiotics are useful for human health. The substandard food consumption causes allergy, cancer, food poisoning, obesity and cardiovascular diseases due to poor dietetic values of provided nutrients². According to the Metchnikoff, probiotics are the microorganisms which have the ability to change the microbial mixture in the entire human body. Studies have revealed that the oral administration of probiotics twist can treat infantile diarrhea in the children of early age. In view of WHO, probiotics are living microorganisms that promote health benefits by increasing or re-establishing the intestinal flora supportive for better intestinal activity³. The vast clinical based researches have emphasized on the positive aspects of probiotics in the treatment of illness like chronic cholera syndrome, gastrointestinal disorders, helicobacter removal, diarrhea, uncontrolled fats, antibiotic resistance, controlling diabetes. The report shows the usefulness of probiotics in various types of cancers and other side effects⁴. WHO has identified probiotics as a non-viable nutritional supplement that provides the host with the health benefits by modulating the microbiota. The factor which determines the disease that leads the appearance and propagation of the disease is called the virulence factor for that one⁵. Pathogens adopt a number of
different mechanisms which trigger the progression of chaos in the human by producing a variety of biological molecules to combat with host to give extraordinary reactions. Thus, virulence is the scrupulous ability of any microorganisms being to infect the host to bring anomalous change in normal conditions. "Virulence" is a Latin word means "poisoned". Strategies used for the devastation of pathogens includes inhibition of transcription in pathogenic microorganism, antimicrobial bacteria, bacteriocins, competition for host dwelling, effects on antioxidant activity, ion disinfection, antiviral and antimicrobial sites. Despite the fact that a lot of work has been done to check the potential of different microbes to improve human health, little is discussed about their role against causative agents in the disease manifestation. We are living in the age of antibiotic resistance, a stronger interpretation of the complex associations of probiotics and pathogens is essential for development of strategies which work effectively in controlling the common infections of current time.

**Probiotics in Infection Treatment:**

Live organisms are known as probiotics which provide health benefits to the host when given in adequate amounts. Various types of probiotics play their role in fermented eatables, tablets, powders and oral drops. These probiotics are easily available in the form of foodstuffs and pharmacies. In the last two decades few drugs as well as probiotics have been tested for human diseases to make comparison. A meta-analysis consisting of 52 reports has revealed the probiotic activities ranges from necrosis in children to constipation and diarrheal infections including liver disorders in adults. Following are the adapted treatment strategies by using probiotics prove their efficiency:

1. Necrotizing enter colitis
2. Acute diarrhea contagious
3. Infections of the lungs
4. Diarrhea associated with antibiotics
5. Infant colitis
6. Allergic disorders

**Necrotizing Enter Colitis (NCE):**

Necrotizing enter colitis is a fatal gastrointestinal tract disease in preterm infants. Children are born with 500-1500 grams weight and about 50% of these cases need surgery afterwards. It is a classical disease linked with gastrointestinal dysbiosis. This is the main reason behind short bowel syndrome. Use of multispecies Lactobacillus and Bifidobacterium probiotics was associated with a significantly decreased risk of NEC. Probiotic therapy exert beneficial effects on NEC in preterm neonates. Probiotic follows different mechanisms in the preterm gastrointestinal tract including upregulation of cytoprotective genes, downregulation of pro-inflammatory gene expression, production of butyrate and other short-chain fatty acids that lower the pH and oxygen tension within the intestinal lumen thereby suppressing the growth of pathogenic Enterobacteriaceae, support of barrier maturation and function and regulation of cellular immunity and Th1:Th2 balance.

**Acute Diarrhea:**

Diarrhea is proven to be one of the major infectious causes of children mortality under five years of age. Acute diarrhea is typically infectious, and in children chances of infection are high in early age 6-24 months. The most common cause of severe and fatal diarrhoea worldwide is rotavirus (associated with 28% of severe cases and 28% of fatal cases), these numbers were reduced in 2011 due to vaccination. V cholerae causes roughly 1% of severe diarrhoea world wide, but is endemic in south Asia and some countries in sub-Saharan Africa. Other viruses (including norovirus, astrovirus, and adenovirus) and bacteria (pathogenic Escherichia coli, Shigella, Campylobacter, and Salmonella) can cause severe diarrhoea but cannot be prevented by vaccines. Poor sanitation and unhealthy hygiene, unpasteurized dairy products causes the
infection that leads to diarrheal dehydrations in infants. Different species of bacteria have studied to minimize the disease chances.

**Acute Infections of the Respiratory Tract:**
All probiotics elicit immune responses when comes in contact with normal body cell of respiratory system. Studies have reported the efficiency by 25% in children to minimize the condition. Lactobacillus GG administration for 28 days after vaccination is found to enhance immune response of the host against influenza virus when compared with only vaccinated patient. Systematic testing has emphasized on reduction in symptoms of disease.

**Antibiotic Associated Diarrhea:**
The AAD is very mild infection caused by drugs, but affects 11% of babies fewer than two years old who were treated with antibiotics. The most effective ADD probiotic in children is Lactobacillus. Bifid bacilli is often more effective in the treatment of ADD in conjunction with other probiotics. AAD may occur after a few weeks or even months after the administration of the antibiotic drugs. Any antibiotic against the anaerobes (aminopenicillins, cephalosporins, clindamycin) has higher risk of infection. Almost every intravenous and oral drug can cause AAD.

**Infant Colitis:**
Infants get this condition at early age of 3 weeks as they cries for many hours regularly. Up to 10% of average infants are infected. Colic may be an abuse and infanticide factor for infants. The function of a single probiotic, L. reuteri has been well studied to control the infection. Now the crying time span can be reduced by about an hour daily in about two weeks with the help of probiotics.

**Allergic Disorders:**
Beneficial microbes also show activity against allergens and in immune response regulation. The probiotics prevent active dermatitis, asthma and allergies to food.

**C: Antivirulent Activity of Probiotics:**
The probiotics modulates the virulence factors of a pathogens through different types of mechanisms adapted which includes disruption of Quorum Sensing, toxin neutralization and colonization resistance.

- **Quorum Sensing Inhibition:**
  Bacteria rely on chemical communication to fellow cells called quorum sensing to ensure that cellular activities are being performed in order along with their survival as well as biofilm formation. It has been seen that whole corresponding expressions of almost all virulence determinants during the process of infectious propagation in synchronized by quorum sensing system. Some compounds (organic acids) have been identified which have inhibitory effects on quorum sensing are secreted by probiotics which are known as quorum sensing inhibitors and are active in producing multidrug resistance in P. aeruginosa and S. aureus strains. The QS system offers a comprehensive and integrated presentation of multiple decisions during disease management. Many additives have been reported in the QS system and are known as QS agents. A study performed by have shown that expression of quorum sensing genes was reduced considerably when P. aeruginosa strains were cultivated in the presence of disinfected probiotic culture filtrate. The particular combination of probiotics has shown the enhanced ability to inhibit the pathogen's adherence to intestinal mucosa when comparison was made to single strains of probiotics. The antibiofilm outcome of L. pentosus and L. plantarum against foodborne pathogen (B. cereus) and plant pathogen (P. aeruginosa) along with dental pathogens Aggregatibacter actinomycetemcomitans, Prevotella melaninogenica, Porphyrmonas gingivalis is up to the mark.

- **Anti Toxin Effects**
  As representatives of the microbial pathogen, toxic bacteria are an important factor in virus
Invasion from the host epithelial cell is a necessary prerequisite for any pathogen to settle a fruitful infection. Epithelial gastric invasion plays a main role in productive stopping of the infection. In summation to producing various antibacterial agents, the probiotics can directly interfere with bacterial infections in the tissues of the stomach. When combined with E.coli nissle (EcN) strain with S. Tjyhimurium, the bactericidal effect was reduced by 70% 35. In the study the author has shown that EcN ability to restrain the invasion of some pathogens of gut like Shigella flexneri, L. monocytogenes and Y. enterocolitica devoid of effecting the viability of agents. The intermingling of EcN with bacterial invasion was observed as mediated by the components secreted by probiotics 36. It is being seen that enhanced potential of bifidobacterial strains is observed effective for the prevention of listeriosis in humans 37.

**Conclusion:**
With the passage of time research and analysis has created an opportunity to develop more advanced, close to nature, economical and efficient remedy to deal with the vital organ disorders in an effective way. The probiotic along with prebiotics and synbiotics are accumulatively a better option to cope the requirements of digestive as well as hepatic remediation to work and run the whole system. These are proving balancing in the regards of treatment without side effects for which earlier was not possible to tackle it purposefully. It was a matter of delightedness to produce such a remedy for what people were waiting for, due to natural combating tendency to restore normal microbial population in the specific tracts its more appropriate and reliable source with reliable potential to be manipulated in the future for more tasks related to health. In the near future we may expect to turn our dream into reality for the processes to deal with such issues very accurately for the cases of pediatric and neonates health chaos for the reason of their absence of negative impacts.

**Anti-Invasion Effects:**
Invasion from the host epithelial cell is a necessary prerequisite for any pathogen to settle a fruitful infection. Epithelial gastric invasion plays a main role in productive stopping of the infection. In summation to producing various antibacterial agents, the probiotics can directly interfere with bacterial infections in the tissues of the stomach. When combined with E.coli nissle (EcN) strain with S. Tjyhimurium, the bactericidal effect was reduced by 70% 35. In the study the author has shown that EcN ability to restrain the invasion of some pathogens of gut like Shigella flexneri, L. monocytogenes and Y. enterocolitica devoid of effecting the viability of agents. The intermingling of EcN with bacterial invasion was observed as mediated by the components secreted by probiotics 36. It is being seen that enhanced potential of bifidobacterial strains is observed effective for the prevention of listeriosis in humans 37.
the enhanced effects hope this strategy will change totally the adaptations for recovery from disease in children as well as in adults due to making no any interference with the working functions of other systems although working in accordance with each other.

References:


17- LaRocque, R.; Harris, J.B. Approach to the adult with acute diarrhea in resource rich setting. UpToDate 2020.


Collado, M.C.; Meriluoto, J.; Salminen, S. Development of new probiotics by strain combinations; is it possible to improve the adherence to intestinal mucosa? Journal of dairy science 2007, 90 (6), 2710-2716.


