WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 7, 2492-2501. Review Article ISSN 2277– 7105

A REVIEW ON PROBIOTICS: AS A PREVENTIVE MEASURE IN DIARRHEA

Indrajeet Pawar*, Prof. Prashant Khade and Dr. Ashok Bhosale

Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre, Kharadi, Pune-14.

Article Received on
21 May 2020,

Revised on 11 June 2020,
Accepted on 02 July 2020,

DOI: 10.20959/wjpr20207-18020

***Corresponding Author**
Indrajeet Pawar
Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre, Kharadi, Pune-14.

ABSTRACT

Probiotics may have preventive or therapeutic effects on diarrhea of various etiologies. However, not all probiotics are effective and physicians must select preparations with proven efficacy. Here, we critically appraise recent data on the prevention and treatment of diarrhea in relation to cause. We also briefly discuss new data impinging on the mechanisms governing the effects of probiotics. The role of probiotics in diarrhea associated with inflammatory bowel diseases and irritable bowel syndrome is not taken into account in this review.

KEYWORDS: Probiotics, Diarrhea, RCT, Progermina.

INTRODUCTION

The probiotic suggests that merely life for originating from the Greek words “pro” and “bios.”[1] The foremost ordinarily quote that means was created by Fuller (1989). The probiotics square measure live microbic feed supplement that beneficially affects the host animal by rising its enteric balance. This correct definition continues to be ordinarily brought up, despite continual competition. Today, probiotics square measure quite on a daily basis in health-promoting “functional foods” for humans, similarly as therapeutic, prophylactic growth supplements in animal production human health.[2-4] alternative ordinarily studied probiotics embrace the spore-forming Bacillus spp. Yeasts are shown to possess adhesion talents, turn out bio activated molecules give immunostimulation.[5-7]

Mechanisms of action of probiotics

Probiotic bacteria can inhibit pathogens by the production of antagonistic compounds/by competitive exclusion (competition for nutrients attachment sites). Probiotic bacteria directly

take up or decompose the organic matter and improve the water quality of an aquatic ecosystem. Beneficial microbial cultures produce a variety of exoenzymes such as amylase, protease, and lipase, which help to degrade the unconsumed feed feces in the pond, in addition to the possible role of these enzymes in the nutrition of the animals by improving feed digestibility and feed utilization. Among all the microbial interventions to augment the production, use of probiotics is in the central dogma. The modes of action of probiotics include the inhibition of a pathogen through the production of bacteriocin-like compounds, competition for attachment sites, competition for nutrients (particularly iron in marine microbes), alteration of the enzymatic activity of pathogens, immunostimulatory functions, and nutritional benefits such as improving feed digestibility and utilization [Figure 1].[5,6,7]

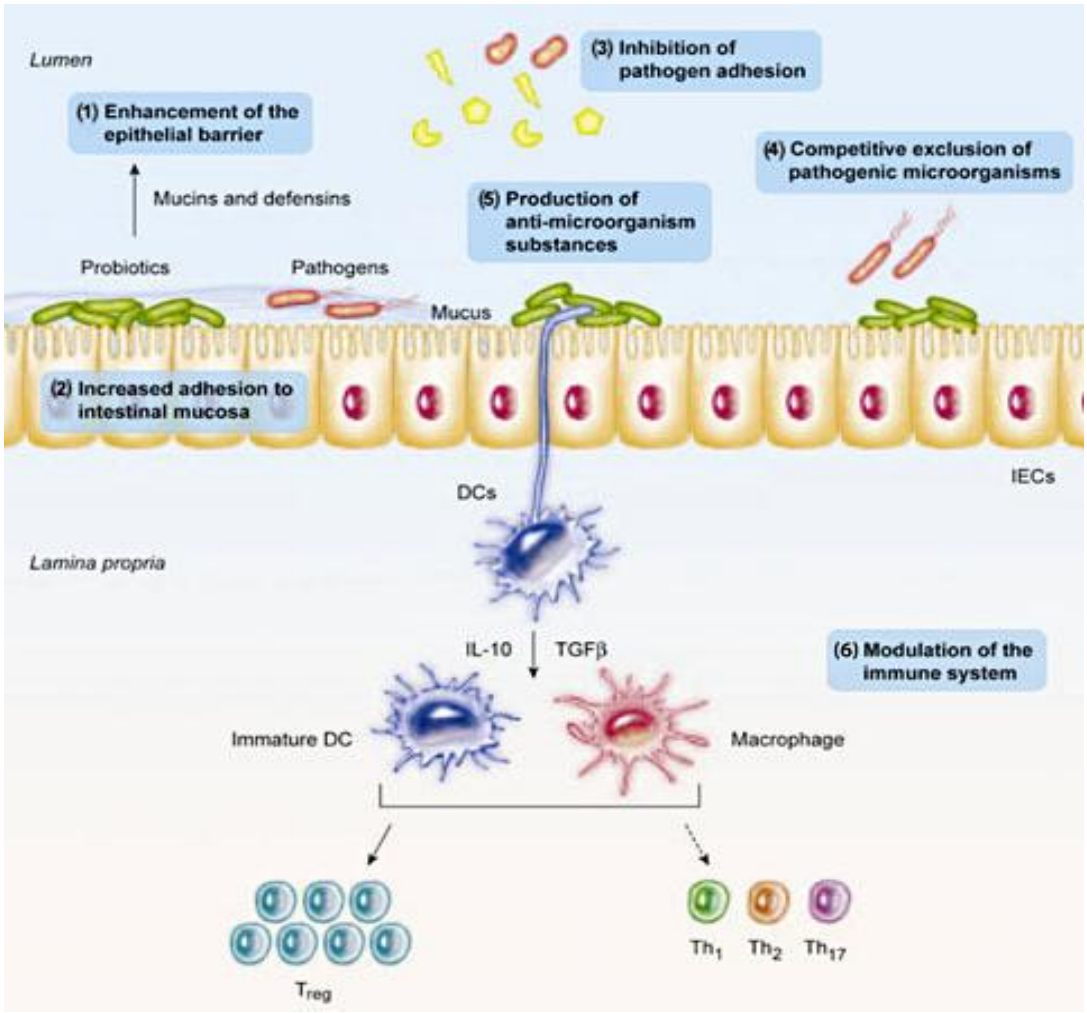

Figure 1: Mechanism of action of Probiotics.

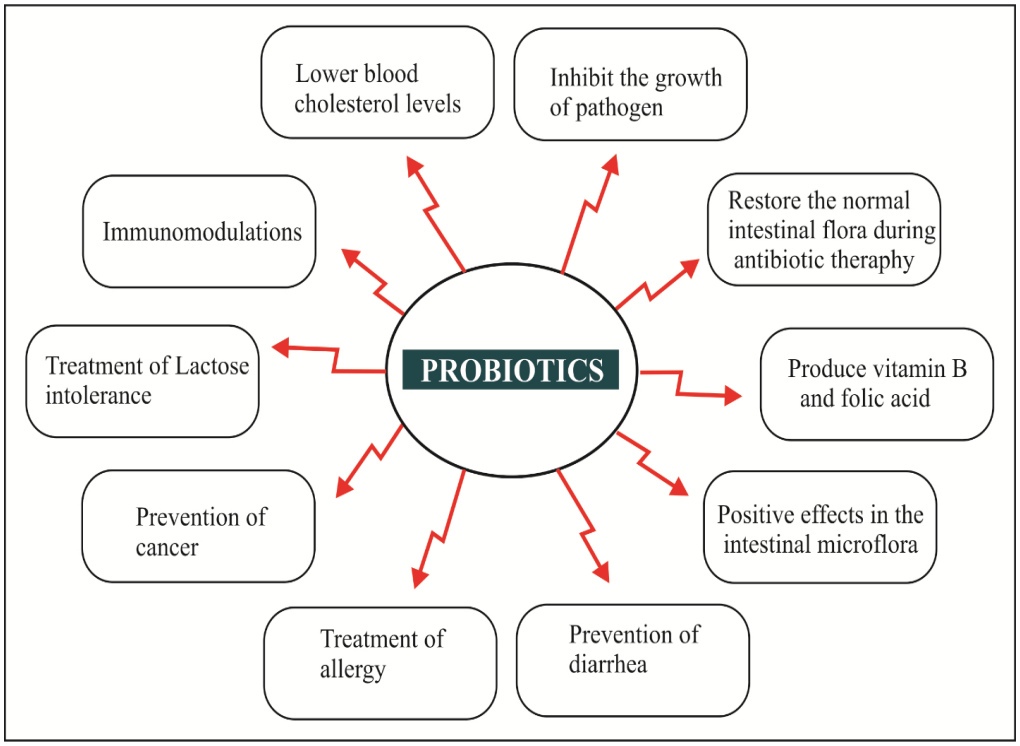

Figure 2: Beneficial effects of probiotics on human health modified from Gibson and Roberfroid.[8]

Prevention of Diarrhea

Probiotics may have preventive or therapeutic effects on diarrhea of various etiologies. However, not all probiotics are effective and physicians must select preparations with proven efficacy.

I. Primary prevention: As diarrhea is a very frequent problem in young infants and children, probiotics have been proposed for the prevention of community-acquired diarrhea. Six randomized controlled trials (RCTs) are available. The probiotics tested were Lactobacillus GG (LGG), Streptococcus thermophilus in association with Bifidobacterium breve or with Bifidobacterium lactis, B. lactis alone, Lactobacillus casei DN-114 and Lactobacillus reuteri. The results were not always statistically significant and were of questionable clinical relevance. A double-blind RCT performed in a large pediatric population in France reported fewer episodes of dehydration, medical consultation and need for formula shift in infants fed probioticsupplemented formula, although the incidence of diarrhea was similar to that of the control group.[9] A smaller RCT in Israel found a reduction in the frequency and duration of diarrhea in treated children.[10] These trials provided evidence of a modest protective effect of specific strains. Indirect evidence that targeting intestinal microecology is effective in preventing diarrhea is the finding of fewer intestinal infections in a cohort of healthy infants

fed prebiotics in the first year of life.[11] The cost efficacy of such interventions remains to be established.

II. Secondary prevention: Secondary prevention involves selected conditions, limited in duration, that are associated with an increased risk of diarrhea rather than with host-related.

Antibiotic-associated diarrhea: Antibiotic-associated diarrhea (AAD) occurs in about 5–25% of adult patients and 11–40% of children upon administration of broad-spectrum antibiotics. Clostridium difficile is a major agent, although diarrhea may be related to general changes in intestinal microflora. A systematic review.[12] and a meta-analysis of RCTs.[13] provided evidence of a moderate beneficial effect of LGG, Saccharomyces boulardii and a combination of B. lactis and S. thermophilus in preventing AAD. A recent Cochrane review of 10 RCTs carried out in 1015 treated and 971 control children reported a significant reduction in the incidence of AAD [Relative risk (RR) 0.49; 95% confidence interval (CI) 0.32–0.74], confirming the efficacy of LGG and S. boulardii.[14] The subgroup analyses provided evidence that probiotic dose may be responsible for the observed clinical and statistical heterogeneity of results. Interestingly, of the eight studies that provided dosage information, five studies in which children received 5–40 billion bacteria/yeast/ day showed that probiotics had preventive effects (RR 0.35; 95% CI 0.25 to 0.47), whereas the combined results of three studies using less than 5 billion colony-forming unit (CFU) bacteria/yeast/day were not significant (RR 0.89; 95% CI 0.53 to 1.48, I2 ¼ 61.4%). The number-needed-to-treat was between seven and 10. As suggested by the Cochrane review, more data are needed to consider the routine use of probiotics to prevent AAD in children started on large spectrum antibiotics. In particular, cost-benefit data are strongly needed.

Two recent double-blind RCTs suggested that other strains were effective in preventing AAD. The first, conducted on 135 adults, showed that a drink containing L. casei, Lactobacillus bulgaricus and S. thermophilus twice daily prevented AAD and diarrhea caused by C. difficile (number-needed-to-treat five and seven, respectively).[15] The second was a pediatric trial in which Lactobacillus rhamnosus (strains E/N, Oxy and Pen) reduced the risk of any diarrhea in children undergoing antimicrobial therapy for common infectious diseases.[16]

The role of probiotics in C. difficile-associated diarrhea is still unclear. S. boulardii was found to be significantly effective in treating C. difficile diarrhea.[17] The benefit of probiotics

in C. difficile diarrhea was mostly seen in adults and, particularly, in subgroups characterized by severe disease.[18] Despite the moderate evidence obtained in adults, the use of probotics to specifically treat or prevent C. difficile diarrhea has not been evaluated in a RCT in children. A recent meta-analysis showed that LGG and S. boulardii might be useful in treating or preventing recurrences of C. difficile diarrhea.[19] Nonetheless, the heterogeneity of the studies makes it difficult to draw definite conclusions.

Nosocomial and day-care center diarrhea: Nosocomial diarrhea may prolong hospital stay and increase medical costs. It is commonly caused by Rotavirus and less frequently by C. difficile. Earlier and inconsistent data suggesting that probiotics may reduce the risk of nosocomial diarrhea were summarized in a recent review, and the conflicting results may have been related to the strain and dose of probiotic used.[20] Five RCTs have been published on the prevention of diarrhea in daycare centers. The probiotics tested were LGG, B. lactis (alone or combined with S. thermophilus) and Lactobacillus thermophilus. Efficacy was modest and inconsistent and was detected for some strains only. A narrative review[20] and a recent systematic review.[21] agreed that evidence in favor of probiotics for prevention of diarrhea in day-care centers and for nosocomial diarrhea is not sufficient to recommend their routine use.

Traveler's diarrhea: Travel is a risk factor for infectious gastroenteritis. A recent meta-analysis revealed evidence of a protective effect by S. boulardi and by mixture of Lactobacillus acidophilus and Bifidobacterium bifidum.[22] However, evidence of the efficacy of probiotics in the prevention of traveler's diarrhea is preliminary.

Diarrhea related to nonantibiotic treatment: Drugs and other treatment administered for noninfectious diseases such as cancer may induce diarrhea. A novel field of application of probiotics is prevention of iatrogenic diarrhea related to treatment toxicity. Lactic acid producing bacteria reduce the risk of radiationinduced diarrhea. Prophylactic administration of VSL#3 (a mixture of four species of lactobacilli, three species of bifidobacteria and S. thermophilus) reduced the incidence of radiation-associated enteritis in a placebocontrolled trial that included 500 patients who underwent postoperative radiation therapy.[23] Some probiotic strains were found to be beneficial in cancer druginduced diarrheas, namely, VSL#3 prevented irinotecan-related diarrhea (in rats) and LGG reduced the frequency of severe diarrhea caused by 5FU-based chemotherapy.[24]

Treatment of intestinal infections: Although the standard treatment of acute diarrhea remains to be an oral rehydration solution (ORS), probiotics have gained an important role as adjuvant therapy. A large number of trials, including randomized and controlled, and several accurate meta-analyses reported that probiotics exerted antidiarrheal effects particularly in children. A wide pattern of strains, schedules, doses and conditions have been tested. The outcomes most widely considered were duration of diarrhea, duration of hospitalization and severity of diarrhea, with some trials evaluating ORS intake, number of vomiting episodes and Probiotics as prevention and treatment for diarrhea Guarino et al. 19 stool volumes. Despite the broad spectrum of design and conditions, nearly all studies showed some positive effects on diarrhea, with statistically significant benefits or moderate clinical benefits mainly in infants and young children. A number of strains have been tested, but proof of efficacy is compelling only for a few. LGG and S. boulardii are the strains most widely tested and also are the most effective. The efficacy of LGG as an adjunctive treatment of diarrhea is now considered conclusive.

PROGERMINA

Progermina Oral Suspension 5ml[25]

Progermina Suspension contains Bacillus clausii as an active ingredient. Progermina suspension has a role in enhancing digestive health. The efficacy of Bacillus clausii, a spore-forming probiotic helps in the treatment of diarrhea, prevention of antibiotic- associated diarrhea, and in the prevention of side effects associated with Helicobacter pylori.

Key benefits/uses of Progermina Suspension

- Bacillus clausii spores and cells can adhere to the bowel wall and colonize the mucosa.
- B. clausii is extremely stable to acidic conditions.
- The entire dose of ingested bacteria reaches the small intestine intact.
- Reduces morbidity and mortality among adults and children globally.

Direction for use/Dosage

- The suspension should be administered twice or thrice (1- 2 teaspoonful) daily or as directed by the physician.

Storage instruction

- Store in a cool, dry and dark place.
- Protect from the direct sunlight.

- Store in the original package in order to protect from moisture.

Safety information

- Keep out of the reach and sight of children.
- Do not exceed the recommended dose.

Uses of Progermina solution on diarrhea

- **Acute diarrhea**

This medicine is used for the treatment of acute diarrhea (less than 14 days old) caused due to infections, medicines, poisonous substances, etc.

- **Chronic diarrhea**

This medicine is used for the treatment of chronic or persistent diarrhea which is more than 14 days old.

Composition: Each 5 ml of Progermina oral suspension contains: *Bacillus clausii* spores... 2 x10^9 and Purified Water IP.....q.s.

Indications: Progermina is indicated for restoration of the alteredintestinal bacterial flora.

Dosage and Administration: Adult:Swallow the contents of 2 – 3 tubes per day; Children: Swallow the contents of1 – 2 tubes per day.

Contraindications: Should not be used in individuals hypersensitiveto the active ingredients.

SideEffects and Special Precautions: Noadverse effects have been reported. If any undesired effect is observedpromptly report to your doctor. *(Fordetailed information please*

write to Zuventus Healthcare Limited, 5119, 5th floor, D-Wing, Oberoi Garden Estates, Chandivali, Andheri (E), Mumbai 400 072 or email to medico@zuventus.com).

REFERNCES

1. Gismondo MR, Drago L, Lombardi A. Review of probiotics available to modify gastrointestinal flora. Int J Antimicrob Agents, 1999; 12: 287-92.
2. FullerR. Probiotics in man and animals. JAppl Bacteriol, 1989; 66: 365-78.
3. Mombelli B, Gismondo MR. The use of probiotics in medical practice. Int J Antimicrob Agent, 2000; 16: 531-6.
4. Ouwehand AC, Kirjavainen PV, Shortt C, Salminen S. Probiotics: Mechanisms and established effects. Int Dairy J., 1999; 9: 43-52. 5. Sullivan A, Nord CE.
5. Kesarcodi-Watson A, Kaspar H, Lategan MJ, Gibson L. Probiotics in aquaculture: The need, principles and mechanisms of action and screening processes. Aquaculture, 2008; 274: 1-14.
6. Demain AL, Sanchez S. Microbial drug discovery: 80 years of progress. J Antibiot (Tokyo), 2009; 62: 5-16. 7. Gill HS, Guarner F. Probiotics and human health: A clinical perspective. Postgrad Med J., 2004; 80: 516-26.
7. Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. J Nutr., 1995; 125: 1401-12.
8. Thibault H, Aubert-Jacquin C, Goulet O. Effects of long-term consumption of a fermented infant formula (with Bifidobacterium breve c50 and Streptococcus thermophilus 065) on acute diarrhea in healthy infants. J Pediatr Gastroenterol Nutr., 2004; 39: 147–152.
9. Weizman Z, Asli G, Alsheikh A. Effect of a probiotic infant formula on infections in child care centers: comparison of two probiotic agents. Pediatric, 2005; 115: 5–9.
10. Bruzzese E, Volpicelli M, Squaglia M, et al. Impact of prebiotics on human health. Dig Liver Dis., 2006; 38(2): S283–S287.
11. Szajewska H, Setty M, Mrukowicz J, et al. Probiotics in gastrointestinal diseases in children: hard and not-so-hard evidence of efficacy. J Pediatr Gastroenterol Nutr., 2006; 42: 454–475.
12. Szajewska H, Ruszczynski M, Radzikowski A. Probiotics in the prevention of antibiotic-associated diarrhea in children: a meta-analysis of randomized controlled trials. J Pediatr, 2006; 149: 367–372.

13. Johnston BC, Supina AL, Ospina M, et al. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. Cochrane Database Syst Rev., 2007; 2: CD004827. A recent and complete systematic review that reports the efficacy of selected probiotics in the prevention of antibiotic-associated diarrhea and underlines the important role of the dose-response effect.
14. Hickson M, D'Souza AL, Muthu N, et al. Use of probiotic Lactobacillus preparation to prevent diarrhoea associated with antibiotics: randomised double blind placebo controlled trial. BMJ., 2007; 335: 80.
15. Ruszczynski M, Radzikowski A, Szajewska H, et al. Clinical trial: effectiveness of Lactobacillus rhamnosus (strains E/N, Oxy and Pen) in the prevention of antibiotic-associated diarrhoea in children. Aliment Pharmacol Ther., 2008; 28: 154–16.
16. A well designed randomized controlledtrialthat demonstratesthe beneficial effects of new probiotic strains for the prevention of antibiotic-associated diarrhea in children.
17. Czerucka D, Piche T, Rampal P. Review article: yeast as probiotics – Saccharomyces boulardii. Aliment Pharmacol Ther., 2007; 26: 767–778.
18. Dendukuri N, Costa V, McGregor M, et al. Probiotic therapy for the prevention and treatment of Clostridium difficile disease: a systematic review. CMAJ, 2005; 173: 167–170.
19. Segarra-Newnham M. Probiotics for Clostridium difficile-associated diarrhea: focus on Lactobacillus rhamnosus GG and Saccharomyces boulardii. Ann Pharmacother, 2007; 41: 1212–1221. Review.
20. Guandalini S. Probiotics for children with diarrhea: an update. J Clin Gastroenterol 2008; 42 (Suppl 2):S53–S57. A complete and useful review that focuses on the efficacy of probiotics for diarrhea of different etiologies in children in different settings.
21. Mrukowicz J, Szajewska H, Vesikari T. Options for the prevention of rotavirus disease other than vaccination. J Pediatr Gastroenterol Nutr., 2008; 46(2): S32–S37.
22. McFarland LV. Meta-analysis of probiotics for the prevention of traveler's diarrhea. Travel Med Infect Dis., 2007; 5: 97–105.
23. Delia P, Sansotta G, Donato V, et al. Use of probiotics for prevention of radiation-induced diarrhea. World J Gastroenterol, 2007; 13: 912–915.
24. Osterlund P, Ruotsalainen T, Korpela R, et al. Lactobacillus supplementation for diarrhoea related to chemotherapy of colorectal cancer: a randomised study. Br J Cancer, 2007; 97: 1028–1034.

25. https://www.omicsonline.org/open-access/bacillus-clausii--the-probiotic-of-choice-in-the-treatment-of-diarrhoea-2157-7595-1000211.pdf