e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(12); 2842-2847

Original Research Article

Efficacy and Safety of Saccharomyces Boulardii (CNCM I-745) In Acute Diarrhea among Children Aged 6 Months to 5 Years: A Double-Blind Randomized Controlled Trial from Western India

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Received: 01-09-2025 / Revised: 15-10-2025 / Accepted: 21-11-2025

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Conflict of interest: Nil

Abstract

Background: Acute diarrhea remains a leading cause of under-5 morbidity and mortality globally, with rotavirus and other pathogens driving a substantial burden, especially in low- and middle-income countries. While oral rehydration therapy (ORT) and zinc reduce dehydration and complications, they do not consistently shorten the duration or intensity of diarrhea. Probiotics, notably Saccharomyces boulardii (SB), have demonstrated benefit in pediatric acute gastroenteritis.

Methods: We conducted a double-blind, randomized, placebo-controlled trial at the Department of Pediatrics, Geetanjali Medical College and Hospital (Udaipur), October 2022–March 2024. Children 6 months–5 years with acute watery diarrhea (≥3 loose stools in 24 h) were randomized (1:1) to SB (CNCM I-745) 250 mg twice daily for 5 days plus standard care (ORS and zinc) or identical placebo plus standard care. Primary efficacy outcomes were stool consistency (Bristol types 1–7), amount (small/medium/large), and frequency (number/day) on Days 3 and 6. Safety was assessed by adverse events (AEs). Data were analyzed using χ^2 and independent t-tests ($p<0.05$).

Results: Of 140 randomized (SB n=70; placebo n=70), baseline characteristics were similar (mean age 2.23±1.32 vs 2.48±1.41 years; 50% vs 51.4% male; dehydration "none/some" comparable; all $p>0.05$). Consistency: On Day 3, loose/watery stools (types 6–7) were less frequent in the SB group (44.3%) than in the placebo group (58.6%; $p = 0.024$); by Day 6, types 6–7 were rare in both groups ($p = 0.376$). Amount: Day-3 "large" stools were markedly lower with SB (8.6%) vs placebo (58.6%; $p<0.001$); by Day 6, "small" stools predominated with SB (94.3%) vs placebo (42.9%; $p<0.001$). Frequency: Day-3 frequency of 1 stool/day occurred in 42.9% (SB) vs 14.3% (placebo) (overall $p=0.010$); Day-6 distributions also favoured SB (1–2 stools/day 94.3% vs 60.0%; $p<0.001$). Safety: AEs were infrequent and similar (SB 2.9% vs placebo 4.3%; $p = 1.00$), with no serious adverse events.

Conclusion: In Indian outpatient children with acute watery diarrhea, adjunct S. boulardii (CNCM I-745) accelerated normalization of stool consistency, amount, and frequency by Day 3, with sustained improvements by Day 6, and an excellent safety profile. Findings support the addition of SB to ORS and zinc in routine care, while larger trials with longer follow-up should evaluate durability and pathogen-specific effects.

Keywords: Acute Gastroenteritis; Diarrheal; Saccharomyces Boulardii; Probiotics; Children; Randomized Controlled Trial; India; ORS; Zinc.

Introduction

Acute diarrheal accounts for an estimated 1.5 million deaths annually in children under five and is the second most common cause of death in this age group worldwide [1]. Rotavirus has historically been the leading etiologic agent, with near-universal infection by age five across socioeconomic strata [2].

In India, rotavirus-associated disease continues to generate substantial mortality and healthcare utilization despite vaccine rollout, translating into hundreds of thousands of hospitalizations and

millions of outpatient visits yearly, alongside considerable direct medical expenditures [3]. Diarrhea is clinically defined by the World Health Organization (WHO) as ≥3 loose or watery stools within 24 hours, with aetiology spanning bacteria, viruses, and protozoa. Management centres on prompt rehydration to avert dehydration and electrolyte imbalance [4,5].

ORT and zinc are cornerstone therapies: ORT prevents and treats dehydration, while zinc reduces severity and recurrence; however, neither reliably shortens illness duration or stool output in all settings [6-8]. Consequently, adjuvant therapies aimed at modifying disease course are of interest. Probiotics—live microorganisms impart health benefits when administered in adequate amounts—have been evaluated across pediatric gastrointestinal conditions, including antibiotic-associated diarrhea and acute infectious gastroenteritis [12]. Among available strains, Saccharomyces boulardii, a non-pathogenic yeast distinct from bacterial probiotics, shows consistent efficacy and notable advantages such as intrinsic resistance to antibacterial agents and negligible gene exchange with bacterial flora [14,15].

Randomized trials and meta-analyses from diverse settings suggest Saccharomyces boulardii may reduce duration of diarrhea, stool frequency, and need for hospitalization, with a favorable tolerability profile [14,15]. Yet, strain- and context-specific effects, differences in standard of care (e.g., routine zinc), and regional pathogen spectra underscore the need for robust, contemporary data from Indian pediatric populations. We therefore conducted a double-blind randomized controlled trial (RCT) to evaluate the safety and efficacy of Saccharomyces boulardii (CNCM I-745) as an adjunct to ORS and zinc among children aged 6 months to 5 years presenting with acute watery diarrhea in Western India. Our primary objectives were to quantify effects on stool consistency, amount, and frequency over the initial treatment week and to assess adverse events.

Materials and Methods

Study Design and Setting: Double-blind, randomized, placebo-controlled trial conducted at the Department of Pediatrics, Geetanjali Medical College and Hospital (GMCH), Udaipur, India, from October 2022 to March 2024.

Participants: Inclusion: children aged 6 months–5 years with acute watery diarrhea (≥3 loose stools in the prior 24 hours).

Exclusion: visible blood in stool; severe malnutrition; severe dehydration by WHO criteria; use of antibiotics/probiotics/prebiotics within 2 weeks; acute systemic illness (e.g., sepsis, pneumonia) or chronic disease (e.g., CLD, CKD, CHD); known immunodeficiency or immunosuppressive therapy; unwillingness to participate.

Randomization and Blinding: Eligible participants were randomized 1:1 using computer-generated allocation to receive S. boulardii or placebo. Study sachets were identical in appearance; allocation was concealed from participants, caregivers, investigators, and outcome assessors until database lock.

Interventions: Intervention arm received S. boulardii CNCM I-745, 250 mg orally twice daily for 5 days, in addition to standard therapy (low-osmolarity ORS and zinc per WHO/IAP guidelines). The control arm received an identical placebo (sugar powder) twice daily for 5 days, in addition to standard therapy. Concomitant care followed national/WHO guidelines for nutrition and rehydration.

Outcomes

Primary efficacy outcomes (assessed at Day 3 and Day 6):

1. Stool consistency using the Bristol Stool Form Scale (types 1–7).
2. Stool amount categorized as small/medium/large.
3. Stool frequency (stools/day; categories 1–7).

Safety Outcomes: Frequency and nature of adverse events (AEs) through Day 6.

Sample Size: Based on estimated prevalence and anticipated effect size, 66 participants per group provided 80% power (α=0.05). Allowing 10% attrition, we targeted 70 per group (total N=140).

Statistical Analysis: Analyses used SPSS v21.0. Continuous variables are presented as mean±SD and compared using independent t-tests; categorical variables as n (%) and compared using χ^2 or Fisher's exact tests as appropriate. Two-sided $p<0.05$ denotes statistical significance. The primary analysis used all randomized participants with available outcome data.

Ethics: The study was started after obtaining approval from the Institutional Research Ethics Board of GMCH. Written informed consent was obtained from parents/guardians before enrolment.

Results

Participants and baseline characteristics: A total of 140 children were randomized (SB n=70; placebo n=70) and completed outcome assessments through Day 6. Baseline characteristics were well balanced: mean age 2.23±1.32 vs 2.48±1.41 years (p=0.380); male sex 50.0% vs 51.4% (p=0.866).

Rural/urban residence, socioeconomic strata, presenting fever, vomiting, abdominal pain,

decreased urine output, and dehydration category ("none" vs "some") did not differ significantly between groups (all p>0.05), indicating successful randomization.

Primary outcomes

Stool Consistency: At presentation (Day 0), both groups predominantly had watery stools (Bristol types 6–7). By Day 3, the SB group showed a greater shift toward formed stools: types 6–7 were present in 44.3% vs 58.6% in placebo (p=0.024), with more children achieving type 4 in the SB arm (20.0% vs 4.3%). By Day 6, watery stools had largely resolved in both groups (p=0.376), though the SB arm showed numerically higher proportions of type 3–4.

Stool Amount: On Day 0, most children in both arms had "large" stool volumes (SB 90.0% vs placebo 81.4%; p=0.227). By Day 3, "large" stools were far less frequent in the SB arm (8.6%) than placebo arm (58.6%; p<0.001). On Day 6, "small" stools predominated in SB (94.3%) vs placebo (42.9%; p<0.001), evidencing a more pronounced reduction in stool output.

Stool Frequency: At baseline, distributions were similar (p=0.778). By Day 3, once-daily stool was more common with SB (42.9%) versus placebo (14.3%), with overall distribution significantly favouring SB (p=0.010). By Day 6, 1–2 stools/day were reported in 94.3% of SB vs 60.0% of placebo participants (overall p<0.001).

Safety: Adverse events were uncommon and comparable (SB 2.9% vs placebo 4.3%; p=1.00). No serious adverse events occurred. Reported AEs included transient abdominal pain, vomiting, or weakness (isolated, self-limited).

Table 1: Baseline Characteristics of the Study Population (N=140).

Characteristic	SB (n=70)	Placebo (n=70)	p-value
Age, years, mean±SD	2.23±1.32	2.48±1.41	0.380
Male sex, n (%)	35 (50.0)	36 (51.4)	0.866
Residence, rural, n (%)	34 (48.6)	37 (52.9)	0.735
Socioeconomic status, upper-middle/lower-middle, n (%)	40 (57.1)	40 (57.1)	0.985
Fever at presentation, n (%)	16 (22.9)	26 (37.1)	0.097
Vomiting at presentation, n (%)	19 (27.1)	18 (25.7)	0.848
Abdominal pain, n (%)	6 (8.6)	10 (14.3)	0.426
Decreased urine output, n (%)	10 (14.3)	7 (10.0)	0.605
Dehydration, none/some, n (%)	41/29	39/31	0.864

Table 2: Stool Consistency (Bristol Types) By Study Day.

Day	Category	SB n=70 n (%)	Placebo n=70 n (%)	p-value
0	Types 6–7	70 (100)	70 (100)	0.734
3	Type 4	14 (20.0)	3 (4.3)	
3	Type 5	25 (35.7)	26 (37.1)	**0.024** (overall)
3	Types 6–7	31 (44.3)	41 (58.6)	
6	Types 3–4	65 (92.9)	60 (85.7)	
6	Types 5–6	5 (7.1)	10 (14.3)	0.376 (overall)

Table 3: Stool Amount by Study Day.

Day	Category	SB n=70 n (%)	Placebo n=70 n (%)	p-value
0	Large	63 (90.0)	57 (81.4)	0.227
3	Large	6 (8.6)	41 (58.6)	<0.001
3	Medium	57 (81.4)	16 (22.9)	
6	Small	66 (94.3)	30 (42.9)	<0.001

Table 4: Stool Frequency Categories by Study Day.

Day	1 stool/day	2 stools/day	3–4 stools/day	≥5 stools/day	p-value (overall)
0	0 (0.0)	0 (0.0)	27 (38.6)	43 (61.4)	0.778 (SB vs placebo)
3	30 (42.9)	10 (14.3)	24 (34.3)	6 (8.6)	0.010
6	31 (44.3)	35 (50.0)	4 (5.7)	0 (0.0)	<0.001

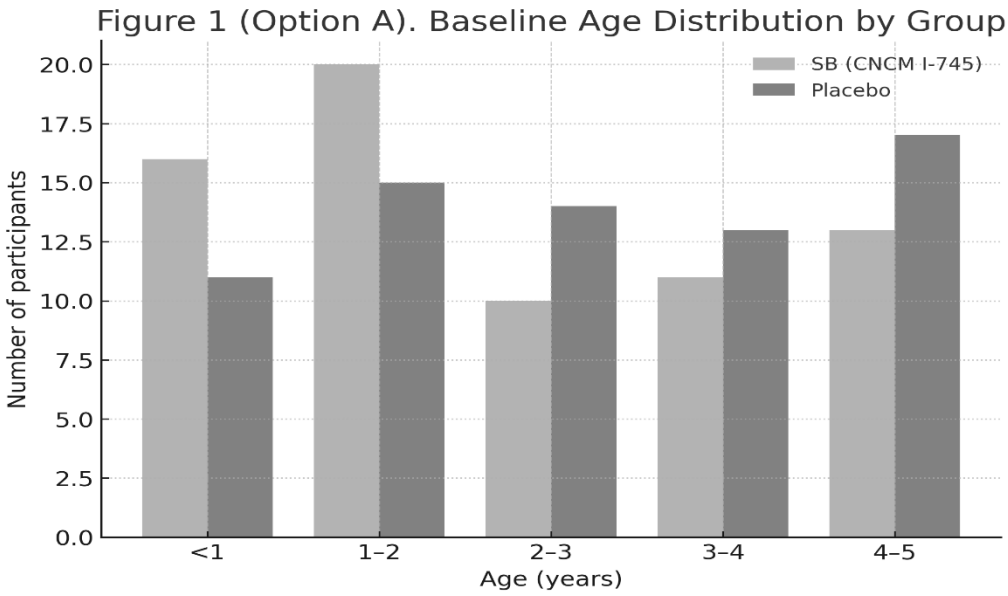

Figure 1: Baseline age distribution by group (SB vs Placebo)

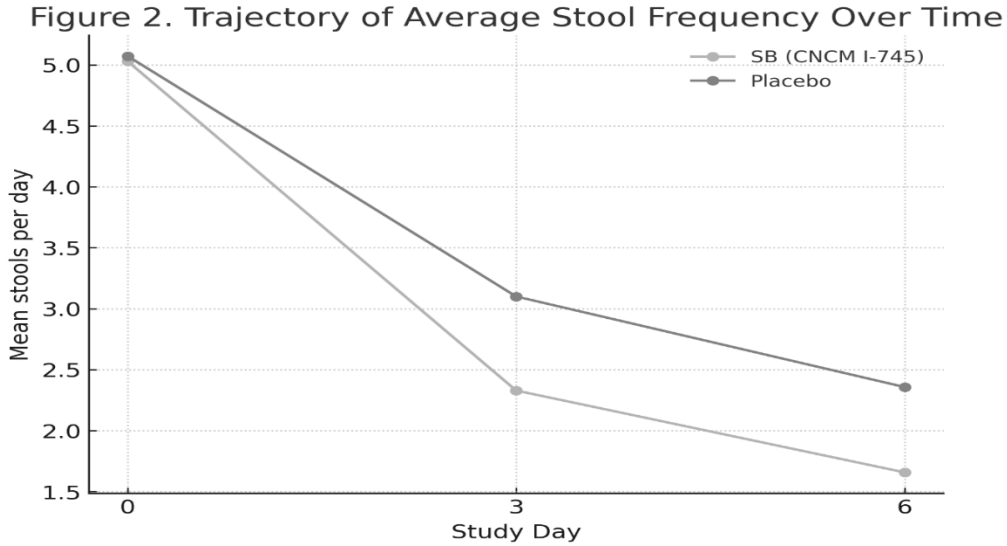

Figure 2: Trajectory of stool frequency over time.

Caption: Median stools/day (IQR) at baseline, Day 3, and Day 6 by treatment arm. SB shows a steeper decline by Day 3 and sustained normalization by Day 6 compared with placebo.

Discussion

In this double-blind randomized trial of Indian children with acute watery diarrhea, adjunct Saccharomyces boulardii (CNCM I-745) produced clinically meaningful improvements in stool consistency, amount, and frequency by Day 3, with sustained normalization by Day 6, compared with placebo given alongside standard therapy (low-osmolarity ORS and zinc). The probiotic was well tolerated, with no serious adverse events. These findings are pertinent given the persistent global and Indian burden of diarrheal illness in children under five and the prominent role of viral aetiologies such as rotavirus [1-4]. Current best practice emphasizes prompt rehydration and appropriate nutrition, with zinc as an important adjunct to reduce severity and subsequent episodes; however, these measures do not reliably shorten the duration or intensity of diarrhea across settings [6-8]. Additional pharmacologic options (e.g., diosmectite) show mixed or population-specific effects and are not universally recommended, particularly in young children, reinforcing the need for safe adjuvants that modify the disease course rather than gut motility [9-11]. In this context, probiotics merit attention. A contemporary Cochrane review concluded that probiotics, as a class, can reduce the duration of acute infectious diarrhea in children, while underscoring strain specificity and heterogeneity across trials [7]. The ESPGHAN Working Group similarly notes conditional support for select strains

in pediatric acute gastroenteritis, emphasizing quality of evidence and product characterization [14]. Broader updates on probiotic health effects also support potential benefits on gut homeostasis and host responses, again with strain-dependent efficacy [12].

Our results align with these syntheses and, more specifically, with prior evidence that S. boulardii reduces stool frequency and shortens illness duration in pediatric gastroenteritis, with a favorable safety profile [15].

As a non-bacterial yeast, S. boulardii has practical advantages in settings where intercurrent or antecedent antibiotic exposure is common, because its viability and activity are not diminished by antibacterial drugs [15]. The early divergence we observed by Day 3 in stool amount and frequency is clinically meaningful for families and services, potentially reducing unscheduled visits and caregiver burden. Importantly, all participants received ORS and zinc per guidance, indicating that the observed effects represent added benefit beyond core therapy [6,8,10,14].

This study has strengths: rigorous blinding, standardized dosing of a well-identified strain (CNCM I-745), pragmatic endpoints that mirror day-to-day recovery, and conduct in an Indian outpatient population where the clinical burden is high [1,3]. Limitations include a single-center design and a sample size sized for clinical (not pathogen-specific) outcomes; we did not collect time-to-resolution in hours or etiologic testing beyond clinical categorization.

Our follow-up ended at Day 6, so durability beyond the first week and effects on re-attendance were not measured. Although safety was excellent here, caution remains appropriate in populations excluded from the trial (e.g., severe malnutrition, severe dehydration, or immunocompromise), consistent with broader safety considerations for probiotics [15]. In practice, adding S. boulardii to ORS and zinc appears reasonable for otherwise healthy children with acute watery diarrhea in outpatient settings, complementing guideline-based care [6,8,10,14]. Future work should include multicenter trials with etiologic stratification, standardized, time-to-event efficacy endpoints, and health-economic evaluation in the Indian context.

Conclusion

In children aged 6 months to 5 years with acute watery diarrhea, adjunct Saccharomyces boulardii (CNCM I-745) given twice daily for 5 days, alongside standard ORS and zinc, significantly accelerated normalization of stool consistency, reduced stool amount, and lowered stool frequency by Day 3, with sustained improvements by Day 6. The probiotic was well tolerated, with no serious adverse events. These data support incorporating S. boulardii as an adjunct in outpatient pediatric diarrhea management in India. Larger, multicentre trials with etiologic stratification and longer follow-up are warranted to confirm durability and generalize findings.

References

1. Walker CLF, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, Black RE. Global burden of childhood pneumonia and diarrhoea. The Lancet 2013; 381(9875):1405–1416.
2. Wilhelmi I, Roman E, & Sánchez-Fauquier A. Viruses causing gastroenteritis. Clinical Microbiology and Infection 2003; 9(4):247–262.
3. Tate JE, Chitambar S, Esposito DH, Sarkar R, Gladstone B, Ramani S. Parashar UD. Disease and economic burden of rotavirus diarrhoea in India. Vaccine 2009; 27(Suppl 5):F18–F24.
4. Ugboko HU, Nwinyi OC, Oranusi SU, Oyewale JO. Childhood diarrhoeal diseases in developing countries. Heliyon 2020; 6(6): e03690.
5. Mahapatro S, Mahilary N, Satapathy AK, Das RR. Nitazoxanide in acute rotavirus diarrhea: A randomized controlled trial from a developing country. Journal of Tropical Medicine 2017; 2017:7942515.
6. Bhatnagar S, Alam S, Gupta P. Management of acute diarrhea: From evidence to policy. Indian Pediatrics 2010; 47(3): 215–217
7. Collinson S, Deans A, Padua-Zamora A, Gregorio GV, Li C, Dans LF, Garner P. Probiotics for treating acute infectious diarrhoea. Cochrane Database of Systematic Reviews 2020; 12, CD003048.
8. Das RR. Zinc in acute childhood diarrhea: Is it universally effective? Indian Journal of Pharmacology 2012; 44(1):140–141.
9. Khediri F, Mrad AI, Azzouz M, Doughi H, Najjar T, Mathiex-Fortunet H, Fekih MA. Efficacy of diosmectite (Smecta) in the treatment of acute watery diarrhoea in adults: A multicentre, randomized, double-blind, placebo-controlled, parallel-group study. Gastroenterology Research and Practice 2011; 783196.
10. Guarino A, Dupont C, Gorelov AV, Gottrand F, Lee JK, Lin Z, Lo Vecchio A. The management of acute diarrhea in children in developed and developing areas: From evidence-based to clinical practice. Expert Opinion on Pharmacotherapy 2012; 13(1): 17–26.
11. Das RR, Sankar J, Naik SS. Efficacy and safety of Dio smectite in acute childhood diarrhoea: A meta-analysis. Archives of Disease in Childhood 2015; 100(7):704–712.
12. Maftei NM, Raileanu CR, Balta AA, Ambrose L, Boev M, Marin DB, Petcu AC. The potential

impact of probiotics on human health: An update on their health-promoting properties. Microorganisms 2024; 12(2): 234.
13. Das RR. Probiotics in necrotizing enterocolitis: More questions than answers? Clinical Nutrition. 2012; 31(3):431–432.
14. Szajewska H, Guarino A, Hojsak I, Indrio F, Kolacek S, Shamir R, Vandenplas Y. Use of probiotics for management of acute gastroenteritis: A position paper by the ESPGHAN Working Group for Probiotics and Prebiotics. Journal of Pediatric Gastroenterol ogy and Nutrition 2014; 58(4):531–539.
15. Kelesidis T, Pothoulakis C. Efficacy and safety of the probiotic Saccharomyces boulardii for the prevention and therapy of gastrointestinal disorders. Therapeutic Advances in Gastroenterology. 2012; 5(2):111–125.