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Efficacy of Probiotics in the Treatment of Acute Infectious Diarrhoeal Disease in African Children: A Protocol For Systematic Review and Meta-Analysis

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Abstract

Background: Diarrhoeal disease is a major global health challenge, causing about 1.7 billion cases annually. It is a major contributor to childhood malnutrition, and the World Health Organisation ranks it third among causes of mortality in children under five, with approximately 443,832 deaths yearly.

Objective: To systematically evaluate the impact of probiotic therapy on diarrhoeal morbidity and mortality in African children between 2010 and 2022.

Methods: A search strategy was developed using MeSH, text words and entry terms. Nine databases will be searched: PubMed, Embase, CINAHL, AJOL, Google Scholar, Web of Science, Cochrane Library, Researchgate and Scopus. Only randomised, double-blind, controlled trials retrievable in English will be included. The primary outcome will be the duration of acute diarrhoea in African children receiving probiotics. Secondary outcomes will include effects on fever, hospitalisation, vomiting, stool frequency/volume, and side effects. Studies will be screened, deduplicated, and eligible studies identified using DistillerSR. Methodological, clinical, and statistical heterogeneity will be assessed. Meta-bias will be evaluated using the Cochrane RoB 2 tool. Publication bias will be assessed using funnel plots and Egger's test. Pooled mean differences in diarrhoeal duration will be reported with standard error and 95% CI. Evidence strength will be rated using the GRADE approach.

Discussion: This study will evaluate the efficacy of probiotics in African children, reporting their effects on diarrhoeal duration, fever, hospital stay, vomiting, stool frequency and volume, and adverse effects. It will examine the moderating effects of sociodemographic factors and probiotic species. Findings will be published in peer-reviewed scientific journals.

Systematic Review Registration: This protocol has been registered with PROSPERO, registration number CRD42023416270

Keywords: Africa, Children, Diarrhoeal diseases, Meta-analysis, Probiotics, Systematic review.

Background

The World Health Organisation (WHO) defines diarrhoea as passing three or more loose or watery stools within 24 hours.[1] It results from infection with bacteria, viruses, protozoa, or parasites. The leading causes in African children include Rotavirus, Escherichia coli, Norovirus, Shigella species, enterotoxigenic and Cryptosporidium. [2]

Clinically, diarrhoea presents with frequent watery stools, vomiting, and signs of dehydration such as sunken eyes, dry mouth, and reduced urine output; severe cases may progress to lethargy or shock. Diagnosis is mainly clinical, with stool analysis performed where resources allow.[3] Diarrhoeal disease remains a leading cause of illness and death among children aged 1 to 59 months, with significant health and economic implications [4, 5] It is a persistent public health challenge in low and middle-income countries, where it disproportionately affects young children and is strongly linked to poverty, poor sanitation, inadequate hygiene, and limited access to safe drinking water.[5] In these settings, children under five years of age experience an estimated six to 12 episodes of acute diarrhoea each year, which is about five times more than in high-income countries. The burden is particularly severe in sub-Saharan Africa and South Asia.[5] According to the Global Burden of Disease Study 2020, diarrhoeal disease accounts for over 500,000 deaths annually among children under five, with the majority occurring in resource-limited regions.[6] Although the latest Global Burden of Disease (GBD) estimates released in 2025 indicate a substantial global decline in diarrhoeal incidence, the condition remains a major public health concern, accounting for approximately 51.4 million years of life lost (YLLs) in 2021, with 30.3 million occurring among children under five years of age.[7]

Beyond its contribution to mortality, diarrhoea is a major cause of undernutrition in children. It leads to stunting, wasting, and impaired immune function.[5] In regions where undernutrition is already widespread, recurrent diarrhoea exacerbates morbidity and adversely affects physical and cognitive development.[8] The economic costs are also considerable. In the United States, managing approximately 220,000 diarrhoeal-related hospital admissions in children under five each year is estimated to cost about 2 billion US dollars. [9, 10] When extrapolated to settings with five times the incidence and much lower gross domestic product, the financial burden becomes even more significant, placing added pressure on already overstretched health systems.

Mortality from diarrhoeal diseases is mainly due to dehydration and electrolyte imbalance, which makes oral rehydration therapy (ORT) the cornerstone of management. Current WHO guidelines emphasise the use of oral rehydration therapy using Oral Rehydration Solution (ORS) to replace fluid and electrolyte losses, zinc supplementation for 10 to 14 days, and continued feeding or breastfeeding to prevent malnutrition. [3] Intravenous fluids are recommended for severe dehydration, while antibiotics are reserved for specific bacterial infections such as Shigella dysentery or cholera.

The widespread use of ORT, along with zinc and vitamin A supplementation, has markedly reduced diarrhoeal mortality among children. As a result, there is now a shift toward improving recovery and reducing the duration and severity of illness. This transition is reinforced by the increased uptake of the rotavirus vaccine, which targets one of the most common causes of acute diarrhoea in young children. Emerging evidence also links diarrhoeal disease to gut microbiome dysbiosis, prompting exploration of novel interventions such as probiotics, prebiotics, and

faecal microbiota transplantation to restore microbial balance. [11, 12] In response to this evolving landscape, there is growing interest in adjunctive therapies such as probiotics, particularly in high-income countries, where their use is gaining popularity. While probiotics have demonstrated potential benefits in reducing the duration and severity of diarrhoea, evidence of their effectiveness and utilisation among African children remains limited and inconsistent. [13]

Probiotics are live microorganisms that, when consumed in adequate amounts, provide health benefits to the host beyond basic nutrition. [14, 15] Common probiotic strains include lactic acid bacteria such as Lactobacillus and *Bifidobacterium* species, *Streptococcus thermophilus*, selected strains of *Escherichia coli*, and the nonpathogenic yeast *Saccharomyces boulardii*. Specific strains such as *Lactobacillus rhamnosus* GG, *L. acidophilus*, and *L. reuteri* have been shown primarily in studies conducted in high-income countries to reduce the duration and frequency of diarrhoeal episodes, enhance immune response, and lower the risk of certain infections. [14, 15]

Numerous mechanistic studies show that probiotics act through multiple complementary mechanisms to reduce the incidence, severity, and duration of diarrhoea. Certain probiotic strains, for example, *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*, compete for nutrient-binding sites and reduce pathogen adherence to the gut mucosa, hence inhibiting enteric pathogen growth.[16, 17] They also improve the intestinal mucosal barrier by promoting tighter inter-epithelial junctions and enhancing mucin synthesis, which lowers fluid and electrolyte leakage into the gut lumen.[18] Furthermore, probiotics influence the host immune response by increasing anti-inflammatory cytokines and decreasing pathogen-induced inflammation, lowering the duration of intestinal injury.[18] Finally, some probiotics produce metabolic products (such as short-chain fatty acids) and lower luminal pH, creating a less favourable environment for pathogen growth and enhancing water absorption from the colon.[19] When combined, these pathways provide a plausible biological basis for the observed clinical findings that probiotic therapies can reduce diarrhoea duration and stool frequency in children.

This study aims to evaluate the effect of probiotics on diarrhoeal morbidity and mortality among African children. By synthesising available evidence, it seeks to address a critical gap in paediatric health interventions and contribute to strategies aimed at reducing the burden of diarrhoeal disease in Africa.

Objective:

General Objective

To systematically review and synthesise available evidence on the efficacy of probiotics in the treatment of acute infectious diarrhoeal disease among children in Africa.

Specific Objectives

a. To determine the effect of probiotic therapy on the duration and frequency of diarrhoea in African children with acute infectious diarrhoea.
b. To evaluate the secondary outcomes, including the summary effect size of probiotics on the duration of fever, length of hospitalisation, frequency of readmission, incidence of vomiting, daily stool frequency, stool volume, and the safety profile of the various probiotic strains.
c. To compare the efficacy of different probiotic strains, dosages, and treatment durations reported in included studies.
d. To assess the overall quality and certainty of the evidence using the GRADE approach.

Methods

This protocol is designed to enable robust, reliable, and accurate data synthesis on probiotics and acute diarrhoeal diseases in African children.

Criteria for considering studies for this review

Study design: We will include randomised controlled trials that evaluated the effect of probiotics in the treatment of acute infectious diarrhoea in African children. We will exclude trials with inappropriate allocation, observational studies, case-control studies, cohort studies, reviews, editorials, commentaries, methodological articles, letters to the editor, case reports, and case series.

PICO framework

Participants: We will include studies conducted among African children aged 1-59 months with acute infectious diarrhoeal disease.[1] We will exclude non-African children, diarrhoea in adults, amoebiasis, clostridium difficile-associated diarrhoea, diarrhoea in children infected with HIV, radiation-induced diarrhoea, and chemotherapy-induced diarrhoea.

Intervention: Use of probiotics alone

Comparator: Children with diarrhoea who received standard care in the form of Oral Rehydration Solution, zinc, and/or vitamin A, and/or antibiotics, but who have not taken probiotics.

Outcomes: These will include both critical outcomes (duration of diarrhoeal episodes, length of hospital stay, and daily stool frequency) and important outcomes (incidence of vomiting, reported complications such as acute kidney injury, survival or death, and adverse effects associated with probiotic use).

The study must be retrievable in English.

Information sources

The search will employ sensitive topic-based strategies designed for each database. The search will be carried out in the following databases: PUBMED, EMBASE, CINAHL, RESEARCHGATE, AJOL, GOOGLE SCHOLAR, WEB OF SCIENCE, SCOPUS and COCHRANE CENTRAL. Only RCTs from 2012 to 2022 will be included.

Additional Information Sources

We will contact trialists and other experts in the field to identify any relevant unpublished or ongoing trials related to our topic. We will also seek clarification from study investigators regarding trial eligibility where necessary. For studies with missing or unclear information, particularly those involving blinding or outcome assessment, we will contact the original trial authors to obtain the required data.

Search strategy

The search strategy includes MESH terms, text words and entry terms. Table 1 shows the search strategies as used in PubMed. The same search strategy will be used in other databases with slight modifications. All relevant published and unpublished trials on probiotics will be actively sought.

Data management and screening process

Data will be managed using four main software applications: DistillerSR, Comprehensive Meta-Analysis (CMA) version 3, Microsoft Excel, and EndNote.

The screening process will be conducted in DistillerSR at six levels.

- Level 1 will involve screening of identified studies for the study design. Only RCTs will be accepted.
- Level 2 will involve screening of identified studies in the titles and abstracts using entry terms, keywords, and MeSH terms.
- Level 3 will involve further screening of the contents of articles by reading the full article using the same search strategy.

- Level 4 will involve snowballing of literature on references from included studies.
- Level 5: Studies will be screened at outcome levels to select those that reported the primary outcome with or without secondary outcomes
- Level 6 will involve grey literature that reports primary outcomes and or secondary outcomes.

The total output from the literature search will first be recorded and archived across all databases, after which duplicate records will be removed using DistillerSR's deduplication function.

Table I: Search strategies for the protocol

Database	Search strategy
PubMed	((((((("probiotic s"[All Fields] OR "probiotical"[All Fields] OR "probiotics"[MeSH Terms] OR "probiotics"[All Fields] OR "probiotic"[All Fields] OR ("synbiotics"[MeSH Terms] OR "synbiotics"[All Fields] OR "synbiotic"[All Fields])) AND ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields] OR "child s"[All Fields] OR "children s"[All Fields] OR "childrens"[All Fields] OR "childs"[All Fields])) OR ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields] OR "child s"[All Fields] OR "children s"[All Fields] OR "childrens"[All Fields] OR "childs"[All Fields])) AND (("acute"[All Fields] OR "acutely"[All Fields] OR "acutes"[All Fields]) AND ("diarrhea"[MeSH Terms] OR "diarrhea"[All Fields] OR "diarrheas"[All Fields] OR "diarrhoea"[All Fields] OR "diarrhoeas"[All Fields]))) OR ("gastroenteric"[All Fields] OR "gastroenteritis"[MeSH Terms] OR "gastroenteritis"[All Fields] OR "gastroenteritides"[All Fields])) AND "africa"[MeSH Terms] AND ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomized controlled trial"[All Fields])) AND (2010/1/1:2022/12/31[pdat])
CINAHL	The above strings will be adapted to the database.

Screening and categorisation will be carried out within DistillerSR. Studies that are clearly ineligible will be excluded, while those considered potentially eligible or unclear will proceed to full-text review. At this stage, eligibility will be reassessed, and final inclusion or exclusion decisions will be made. The reasons for excluding studies after full-text review will be documented.

All screenings will be conducted independently and blinded by two reviewers. Their decisions will be compared at the end of each stage, and any disagreements will be resolved by a third, independent reviewer who will act as a tiebreaker.

The entire process, including the number of records identified, screened, included, and excluded, along with the reasons for exclusion, will be summarised in a PRISMA flow diagram.

c. Data Collection

Data items will be extracted from selected studies and entered into predefined forms in DistillerSR. The following items will be extracted:

i. Surname of first author and year of publication (Study ID)
ii. The sociodemographic characteristics of the study participants, such as age, gender, country, and region in Africa.
iii. The duration of diarrhoea.
iv. The duration of fever.
v. The duration of hospitalisation.
vi. The frequency of vomiting.

vii. The number of bowel movements per day.
viii. Volume of diarrhoeic stool.
ix. Frequency of reported side effects of probiotics.
x. Type of probiotic used.
xi. Severity of dehydration.
xii. Use of antibiotics.
xiii. Use of oral rehydration therapy, zinc and/or vitamin A.
xiv. Evidence of acute kidney injury.

Authors of included studies with missing data will be contacted via email and telephone. Data items will be exported in a predefined format to Microsoft Excel and imported into the CMA software for quantitative analysis.

Data synthesis

Extracted data items will be used for both narrative synthesis and quantitative analysis.

The following criteria will be applied for analysis:

a. Studies that meet the methodological quality criteria using the Cochrane Risk of Bias 2 (RoB 2) tool for randomised controlled trials will be cross-validated using an alternative quality assessment tool, such as the Jadad scale or the Physiotherapy Evidence Database (PEDro) scale, to ensure consistency and robustness of the quality appraisal. The results will be presented in tabular format. Indicating all the extractable data items as listed under data collection.

b. Studies providing qualitative data, whether as primary or secondary outcomes, will be included in the narrative synthesis.

c. All studies with primary outcomes and secondary outcomes that pass heterogeneity tests will be used for quantitative synthesis.

d. Further Analysis: Subgroup analysis will be performed using variables such as age, gender, socioeconomic status, geographical location (country), level of education, occupation and species of probiotic used and the effect of other moderators as stated below. Meta-regression will be performed on the safety concerns.

e. Where heterogeneity exists, sensitivity testing using include/exclude functions in the CMA software will be performed.

f. The computational model for analysis is a random effect model since several studies across Africa will be included.

Risk of bias

The risk of bias in the included studies will be assessed for the individual article using the Cochrane Risk of Bias 2 (RoB 2) tool for randomised controlled trials. It will be cross-validated using the Jadad scale or the Physiotherapy Evidence Database (PEDro) scale to ensure consistency and robustness of the quality of appraisal. Publication bias in the selection of studies will be visually assessed using a funnel plot (trim-and-fill method) and a test for asymmetry when the number of trials exceeds 10. Other statistical tests, such as Egger's regression intercept, Begg and Mazumdar's rank correlation and Orwin's fail-safe N, will be used where appropriate. Studies with a high risk of bias will be subjected to sensitivity testing using the include/exclude function in the CMA Software.

In addition to statistical methods for assessing risk of bias, trial investigators will be contacted to clarify aspects of trial design, conduct, and analysis, or to provide additional data when necessary.

Measurement of treatment effect

Data extracted from the included studies will be exported to Comprehensive Meta-Analysis (CMA) version 3, which will be used to convert effect sizes and perform all statistical analyses. Effect estimates for all outcomes will be reported using appropriate summary statistics, depending on the data type and distribution of the data. For continuous outcomes such as duration of diarrhoeal episodes, length of hospital stay, and daily stool frequency, mean differences (MD)

with corresponding 95% CI will be calculated. When studies report outcomes on different scales, standardised mean differences (SMD) with 95% CI will be used to allow comparison across studies. For dichotomous outcomes, including incidence of vomiting, occurrence of complications such as acute kidney injury, survival or death, and adverse effects associated with probiotic use, risk ratios (RR) with 95% CI will be computed.

Pairwise comparisons of treatment effects between the intervention and comparator groups will be performed using random-effects meta-analysis models, accounting for clinical and methodological heterogeneity across studies. Fixed effect models will be used in sensitivity analyses to assess the robustness of the pooled estimates.

The unit of analysis for each outcome will correspond to the individual participant. For studies with multiple intervention arms, relevant groups will be combined to avoid double-counting of participants. When outcome measures are reported in different units, CMA version 3 will be used to convert data to a common metric before analysis. Where conversion is not possible, findings will be summarised narratively.

For qualitative outcomes or studies not suitable for meta-analysis, a narrative synthesis will be conducted, summarising key findings, methodological quality, and consistency of effects across studies.

Assessment of Meta-bias

Meta-bias will be assessed as follows:

i) Types of probiotics

ii) Index of reporting outcomes in studies: Studies that were reported in different indices but similar in outcome and design will be converted to the primary effect size (prevalence) based on individual case evaluation.

iii) Heterogeneity will be assessed at the study level using the Q statistics, and its p-value, I^2, and τ^2 (Tau squared). As a rule of thumb, I^2 values < 40% will be considered low heterogeneity, values > 40 but < 75% moderate, and values > 75% high.

Subgroup Analysis

Subgroup analyses will be conducted to explore trial-level and participant-level factors that may influence the effect of probiotics. These may include the duration of the intervention, probiotic strain and dose, and baseline characteristics of participants. Interactions between these factors and treatment outcomes will be assessed to identify potential effect modifiers and sources of heterogeneity. We will also evaluate the moderating effects of the degree of dehydration, the use of antibiotics, and the type of therapy administered (including Oral Rehydration Solution alone, Oral Rehydration Solution with zinc, or Oral Rehydration Solution with zinc and vitamin A supplementation) on the study outcomes.

Strength of evidence

The strength of evidence for each outcome will be assessed using the GRADE approach, which considers risk of bias, inconsistency, indirectness, imprecision, and publication bias. Each outcome will be rated as high, moderate, low, or very low in certainty, and the findings will be summarised in a GRADE evidence profile.

Presentation and Reporting of Results

The study selection process will be summarised in a PRISMA flow chart, following the PRISMA 2020 Statement and PRISMA-P Checklist. A table of the search strategy across various databases, including text words, MeSH terms, and entry terms, will be included. A list of included studies will be summarised in a table. Quantitative data such as duration of diarrhoea and fever, the duration of hospitalisation, frequency of vomiting, and the number of stools per day and frequency of side effects will be reported with their 95 % CI, P values, and relative

weights assigned to studies, and heterogeneity tests will be included in the forest plots. A table of quality scores and risk of bias of each eligible study will be included. Forest and regression plots will be included to show subgroup analysis and meta-regression, respectively.

Discussion

The effect size for the primary outcome is the reduction in the number of days of diarrhoea with the use of probiotics in the treatment of children with acute diarrhoea. The secondary outcomes will include a summary effect size of the probiotic on the duration of fever, the duration of hospitalisation, vomiting, and the number of daily stools. We will explore the moderating effects of sociodemographic and environmental factors, and the species of probiotics on the primary and secondary outcomes. The outcome of this study will be published in peer-reviewed scientific journals.

List of Abbreviations

PRISMA-P: Preferred Reporting Items for Systematic reviews and
Meta-analyses Protocols
CMA: Comprehensive Meta-Analysis Software

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval/ Dissemination

This study will utilise data from previously published sources; therefore, ethical approval is not required. The findings will provide valuable pooled evidence on the effectiveness and safety of probiotics, contributing to informed, evidence-based management of diarrhoeal diseases in African children. The final report will be submitted for publication in a peer-reviewed journal and disseminated to healthcare providers and policymakers involved in child health across Africa.

Informed Consent

Not applicable

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c. Guarantor of the review: Michael Abel Alao will serve as guarantor for the review.

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References

1. UNICEF, WHO. Diarrhoea: Why children are still dying and what can be done, UNICEF-WHO. New York: UNICEF/WHO 2009. doi, 10, pp.S0140–6736.
2. Peterson KM, Diedrich E, Lavigne J. Strategies for Combating Waterborne Diarrheal Diseases in the Developing World. ES; 2008.
3. Fang Y-H, Wan C-M, Gong S-T, Fang F, Sun M, Qian Y, *et al.* Clinical practice guidelines for acute infectious diarrhoea in children in China (2024). *World J Pediatr* 2025:1-12.
4. Claudine U, Kim JY, Kim E-M, Yong T-S. Association between sociodemographic factors and diarrhoea in children under 5 years in Rwanda. *Korean J Parasitol.* 2021;59(1):61.
5. World Health Organisation. Diarrhoeal disease [Internet]. Geneva: World Health Organisation; 2024 7th March [cited 2025 3rd August]. Available from: https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease.
6. Troeger CE, Khalil IA, Blacker BF, Biehl MH, Albertson SB, Zimsen SRM, *et al.* Quantifying risks and interventions that have

affected the burden of diarrhoea among children younger than 5 years: an analysis of the Global Burden of Disease Study 2017. *Lancet Infect Dis.* 2020;20(1):37-59.

7. Kyu HH, Vongpradith A, Dominguez R-MV, Ma J, Albertson SB, Novotney A, *et al.* Global, regional, and national age-sex-specific burden of diarrhoeal diseases, their risk factors, and aetiologies, 1990–2021, for 204 countries and territories: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet Infect Dis.* 2025;25(5):519-36.
8. Akombi BJ, Agho KE, Merom D, Renzaho AM, Hall JJ. Child malnutrition in sub-Saharan Africa: A meta-analysis of demographic and health surveys (2006-2016). *PLoS ONE.* 2017;12(5):e0177338.
9. Lanata CF, Fischer-Walker CL, Olascoaga AC, Torres CX, Aryee MJ, Black RE, *et al.* Global causes of diarrheal disease mortality in children< 5 years of age: a systematic review. *PLoS ONE.* 2013;8(9):e72788.
10. Walker CLF, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, *et al.* Global burden of childhood pneumonia and diarrhoea. *Lancet.* 2013;381(9875):1405-16.
11. Ramamurthy T, Kumari S, Ghosh A. Diarrheal disease and gut microbiome. *Prog Mol Biol Transl Sci.* 2022;192(1):149-77.
12. Zhang X, Luo X, Tian L, Yue P, Li M, Liu K, *et al.* The gut microbiome dysbiosis and regulation by faecal microbiota transplantation: umbrella review. *Front Microbiol.* 2023;14:1286429.
13. Kambale RM, Nancy FI, Ngaboyeka GA, Kasengi JB, Bindels LB, Van der Linden D. Effects of probiotics and synbiotics on diarrhoea in undernourished children: Systematic review with meta-analysis. *Clin Nutr.* 2021;40(5):3158-69.
14. Feizizadeh S, Salehi-Abargouei A, Akbari V. Efficacy and safety of Saccharomyces boulardii for acute diarrhoea. *Pediatrics.* 2014;134(1):e176-91.
15. Szajewska H, Kołodziej M. Systematic review with meta-analysis: Lactobacillus rhamnosus GG in the prevention of antibiotic-associated diarrhoea in children and adults. *Aliment Pharmacol Ther.* 2015;42(10):1149-57.
16. Team WR. World Gastroenterology Organisation Global Guidelines: Probiotics and prebiotics. World Gastroenterology Organisation. 2017.
17. Wei M, Liu H, Hu Z, Wen P, Ye Y, Chamba Y, *et al.* A Mechanistic Approach to Replacing Antibiotics with Natural Products in the Treatment of Bacterial Diarrhoea. *Biomolecules.* 2025;15(7):1045.
18. Do Carmo MS, Itapary dos Santos C, Araújo MC, Girón JA, Fernandes ES, Monteiro-Neto V. Probiotics, mechanisms of action, and clinical perspectives for diarrhoea management in children. *Food Function*. 2018;9(10):5074-95.
19. Thakur R, Kaur S. Use of postbiotics and parabiotics from lactobacilli in the treatment of infectious diarrhoea. *Microb Pathogenesis.* 2025:107580.