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SUPPLEMENTARY MATERIAL **OPEN ACCESS**

Probiophage: A Novel Candidate for the Treatment of Irritable Bowel Disease (IBD): A Systematic Review

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PRISMA 2009 Checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Article title: "Probiophages: a novel candidate for the treatment of irritable bowel disease (IBD)" - marked as a systematic review.
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	The presented structured abstract includes: background, objectives (investigating the role of probiotics in IBD), methods (systematic review), results (promising preclinical and clinical findings), and conclusions.
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	The introductory section describes the disease trajectory of IBD, microbial dysbiosis, and the limitations of existing treatments (antibiotics, probiotics).
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	The objectives stated in the abstract and introduction are to focus on the therapeutic role of probiotics and their impact on microbial balance and inflammation.
METHODS			

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Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	The review was conducted based on the flow diagram and PICOS table, and there is no registry data base.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Search Strategy section: Inclusion criteria included studies in IBD patients or animal models (2010–2023) with outcomes such as symptom reduction and microbiota changes; non-English studies were excluded.
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Information sources: PubMed, Scopus, Google Scholar searched until 2023.
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Keywords (e.g., IBD, probiotics, bacteriophages) are listed and search explained is in flow diagram.
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	The study selection process is described with the PRISMA diagram (Flow Diagram) and text; screening by multiple investigators and exclusion of irrelevant studies.
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Data extracted via Flow Diagram
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Variables (primary and secondary objectives such as symptom reduction, microbiota changes) are defined.
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Individual risk of bias was not assessed due to diverse study designs and the exploratory nature of included research, limiting the applicability of standardized bias assessment tools.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Key clinical outcomes such as reduction in inflammation are stated, but specific statistical measures or hazard ratios are not stated. Because statistical analysis was not performed in this review.
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	This is a systematic review without a meta-analysis; therefore, heterogeneity indices such as I^2 are not applicable
Section/topic	**#**	**Checklist item**	**Reported on page #**
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Key clinical outcomes such as reduction in inflammation are stated, but specific statistical measures or hazard ratios are not stated. Because statistical analysis was not performed in this review,
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	This is a systematic review without a meta-analysis; therefore, heterogeneity indices such as I^2 are not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	-
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Tables 1 and 2 include phage families, therapeutic approaches, and key studies.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	This review did not assess risk of bias due to diverse study designs and emerging exploratory research, focusing instead on qualitative synthesis of therapeutic insights.
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Results are reported anecdotally and study by study (such as phage-probiotic combinations in colitis models).
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	No quantitative synthesis was performed; the results are summarized in narrative form.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	The review highlights potential publication bias due to preliminary studies with small samples and diverse designs in probiophage therapy for IBD, urging cautious interpretation and need for rigorous future research.
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	No additional analyses or subgroup analyses were performed.
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Discussion of the therapeutic potential of probiotics, limitations (need for clinical trials), and relevance to IBD treatment is highlighted.

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Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Limitations include a lack of large clinical trials, long-term safety data, and a lack of complete understanding of the mechanisms of action.
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Conclusion: Probiophages have been proposed as an innovative treatment and require further investigation.
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	There was no financial source.

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