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The effects of postbiotics on chemically-induced colitis in mice: A protocol for a systematic literature review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - No financial support or sponsor for this research.

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Conflicts of interest - GV is a board member of the International Scientific Association for Probiotics and Prebiotics (ISAPP).

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 October 2023 and was last updated on 04 October 2023.

INTRODUCTION

Review question / Objective The aim of this systematic literature review and meta-analysis is to determine whether postbiotics have beneficial effects on the symptoms of chemically-induced colitis (CIC) in mice.

Rationale As of October 2022, the effects of postbiotics on CIC in mice had not been systematically reviewed. This systematic review will thus help to provide a basis for future studies that focus on the potential of postbiotics in treating inflammatory bowel disease (IBD) in humans.

Condition being studied IBD is a group of chronic relapsing disorders, including Crohn's disease (CD) and ulcerative colitis (UC), that cause inflammation of the gastrointestinal tract (GIT) (Cai et al., 2021). Current treatment options (e.g. surgery) do not reliably cure IBD and are often associated with undesirable side effects and complications (Hazel & O'Connor, 2020; Li & Zhu, 2018). Therefore, further understanding of the disease is required to enable the development of improved, alternative treatment options. A characteristic of IBD is gut dysbiosis, which leads to an imbalanced microbial composition resulting in impaired intestinal barrier function (Ocansey et al., 2019; Qiu et al., 2022). For this reason, it is suggested that potential treatment options for managing IBD in humans could involve the administration of agents, such as prebiotics, probiotics and/or postbiotics, that improve the intestinal microbial ecology (Cai et al., 2021). Here we provide the first systematic review of the effects of postbiotics on CIC in mice.

METHODS

Search strategy A systematic bibliometric search was conducted of the following eight scientific databases: PubMed, SCOPUS, Web of Science,

EBSCOhost, Cochrane Library, PROQUEST, SciFinder and Ovid. PROQUEST covered the grey literature. Each database was searched from inception up to 16/12/2022. In addition, the reference lists of all eligible articles were manually scrutinised for further eligible articles and further citation tracking was conducted on Google Scholar (up to 1st November 2022) to identify any relevant additional papers. This systematic review is restricted to randomised controlled trials (in vivo studies) that investigated the effects of postbiotics on CIC in mice. A search strategy was devised to identify such studies based on two concepts: postbiotics and gut health/disease. The following Boolean operator was used in all the scientific databases: ((postbiotic OR paraprobiotic OR paraprobiotics OR "tyndallized probiotic" OR "non-viable probiotic" OR "non viable probiotic" OR "heat-killed probiotic" OR "heat killed probiotic" OR "heat-killed microorganism" OR "heat killed microorganism" OR metabiotic OR metabiotics OR "non-viable microbial cells" OR "non viable microbial cells" OR "non-viable microbial cell" OR "non viable microbial cell" OR "inanimate microorganism" OR "inanimate microbe" OR "inactivated culture" OR "inactivated microbe" OR "inactivated microorganism" OR "ghost probiotic" OR "ghost probiotics" OR "fermented infant formulas" OR "fermented formula" OR "fermented milk formula") AND (gut OR guts OR "gut health" OR "gut microbiome" OR "gut microbiota" OR "digestive system" OR "digestive disorder" OR "digestive health" OR digestive OR "gastrointestinal tract health" OR "git health" OR "gut barrier" OR ibs OR "irritable bowel syndromes" OR ibd OR "irritable bowel disorders" OR "gastrointestinal disorder" OR "gastrointestinal disorders" OR "intestinal disorder" OR "intestinal disorders" OR diarrhea OR antidiarrheal OR "gastrointestinal tract cancer" OR "colon cancer" OR colitis OR "leaky intestinal barrier" OR "necrotizing enterocolitis" OR "crohn's disease" OR "intestinal antibody response")). No search filters were applied.

Participant or population Mice with chemically induced colitis (no age, strain, sex or weight restrictions).

Intervention Only treatments employing postbiotics (no other interventions) were considered. Postbiotics are defined as the "preparation of inanimate microorganisms and/or their components that confers a health benefit on the host" (Salminen et al., 2021). Hence, non-viable microbiological biomass was required as the intervention agent (with or without corresponding microbial metabolites).

Comparator Mice with CIC but without postbiotic (or any other) intervention.

Study designs to be included Randomised controlled trials (in vivo mice studies).

Eligibility criteria The eligible articles were selected through application of the following PICO model: (P); Mice with chemically induced colitis, (I); Treatment with postbiotics only, (C); No treatment with postbiotics (or anything else), and (O); Clinical outcomes (e.g., histological score, colon length, disease activity index). Additionally, eligibility required that the applied postbiotic was in the form of an inactivated (non-viable) microorganism (according to ISAPP's postbiotic definition). Therefore, studies that used purified metabolites derived from microbes or a mixture of undefined metabolites (e.g. supernatants devoid of microorganisms) were excluded. Also, only studies based on primary research performed in mice (no weight, strain, sex, or age restrictions) that were written in English were included. Lastly, the outcomes were required to be presented (or to be manually convertible) as mean standard deviation. This requirement was imposed to enable the generation of the respective forest plots. Data expressed as median interquartile values were excluded because its conversion to mean standard deviation can be imprecise. The availability of the sample size for each eligible study was also an essential requirement since this criterion was also required for the construction of the forest plots. The eligibility screening was carried out by two researchers (Kleanthous and Barrett), independently.

Information sources PubMed, SCOPUS, Web of Science, EBSCOhost, Cochrane Library, PROQUEST, SciFinder and Ovid databases were searched from inception up until 16/12/2022 to identify all the relevant articles. Additionally, the reference lists of all eligible articles were manually screened and further citation tracking was conducted on Google Scholar (up to 1st November 2022) to identify any relevant additional papers.

Main outcome(s) All relevant histological, biochemical and immunological outcomes were considered for inclusion. Examples are as follow: disease activity index, histological score, colon length, and the gene expression of pro-inflammatory cytokines, anti-inflammatory cytokines, transcription factors and tight junction proteins. All relevant outcomes were considered and a thematic analysis was carried out. Meta-analysis was conducted where a sufficient number of studies (n=4) reported the same outcome.

Additional outcome(s) N/A.

Data management All retrieved studies were imported into a Microsoft Excel file and then duplicates were manually removed. Two researchers (Kleanthous and Barrett) independently screened the titles and abstracts and then the remaining full-text articles were assessed for eligibility. The inclusion and exclusion criteria were followed as previously defined. Any discrepancies were resolved through discussion and third-party adjudication. Statistical analysis was performed by RevMan, Version 5.4.1, software.

Quality assessment / Risk of bias analysis The updated ARRIVE guidelines were followed to evaluate the individual studies. Both the 'ARRIVE Essential 10', and the 'Recommended Set' questionnaires were answered since this represents best practice (Sert et al., 2020). A cumulative score was then calculated by summing each question's score. The individual score for each question was determined by the lead author of this review.

Strategy of data synthesis Statistical analysis was performed using RevMan (Version 5.4.1) software. WebPlotDigitizer (Version 4.6.) was used to extract data when only available graphically. The data type for all of the outcomes was continuous. The statistical method used was the Inverse Variance (IV). Depending on the level of heterogeneity (I(2)), the analysis model was either a fixed or random effect. A fixed effect model was used when I(2) ≤50%, and when I(2) >50%, a random effect model was used. A P-value <0.05 was considered statistically significant.

Subgroup analysis This study performed subgrouping with at least three studies (n=3) in each subgroup in order to explore any potential reasons for high heterogeneity.

Sensitivity analysis No sensitivity analysis was carried out.

Language restriction English only.

Country(ies) involved United Kingdom, Argentina, Cyprus.

Other relevant information This work was based upon a BSc final year project from the University of Reading (School of Biological Sciences) by Chrysanthos Kleanthous. Thus, a preliminary report was already available in the form of a dissertation.

Keywords Postbiotic, chemically-induced colitis, inflammatory bowel disease, IBD, systematic review, mouse model, ISAPP, randomised controlled trial, meta-analysis.

Dissemination plans This systematic review and meta-analysis will be published in a peer-reviewed journal.

Contributions of each author

Author 1 - Chrysanthos Kleanthous - Devised the search strategy, carried out the searches, eligibility screening and meta-analysis of data. Writing the introduction, methods, results, discussion, and conclusions. Revised and approved the final draft.
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References

Cai, Z., Wang, S., & Li, J. (2021). Treatment of Inflammatory Bowel Disease: A Comprehensive Review. Frontiers in Medicine, 8, 765474.

Hazel, K., & O'Connor, A. (2020). Emerging treatments for inflammatory bowel disease. Therapeutic Advances in Chronic Disease, 11, 2040622319899297.

Li, Y., & Zhu, W. (2018). Common Complications of Surgery for Crohn's Disease and Ulcerative Colitis. Interventional Inflammatory Bowel Disease: Endoscopic Management and Treatment of Complications, 273–286.

Ocansey, D. K. W., Wang, L., Wang, J., Yan, Y., Qian, H., Zhang, X., Xu, W., & Mao, F. (2019). Mesenchymal stem cell–gut microbiota interaction in the repair of inflammatory bowel disease: an enhanced therapeutic effect. Clinical and Translational Medicine, 8(1), 31.

Qiu, P., Ishimoto, T., Fu, L., Zhang, J., Zhang, Z., & Liu, Y. (2022). The Gut Microbiota in Inflammatory Bowel Disease. Frontiers in Cellular and Infection Microbiology, 12, 733992.

Salminen, S., Collado, M. C., Endo, A., Hill, C., Lebeer, S., Quigley, E. M. M., Sanders, M. E.,

Shamir, R., Swann, J. R., Szajewska, H., & Vinderola, G. (2021). The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. Nature Reviews Gastroenterology & Hepatology, 18(9), 649–667.

Sert, N. P., Hurst, V., Ahluwalia, A., Alam, S., Avey, M. T., Baker, M., Browne, W. J., Clark, A., Cuthill, I. C., Dirnagl, U., Emerson, M., Garner, P., Holgate, S. T., Howells, D. W., Karp, N. A., Lazic, S. E., Lidster, K., MacCallum, C. J., Macleod, M., Würbel, H. (2020). The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. PLOS Biology, 18(7), e3000410.