

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Pharmacology and Therapeutics*

Manuscript NO: 88566

Title: Effectiveness of an amino acid beverage formulation in diarrhea-predominant irritable bowel syndrome: A pragmatic real-world study

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04451514

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-09-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-01 00:43

Reviewer performed review: 2023-10-01 02:07

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input checked="" type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input checked="" type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

1 Title. Does the title reflect the main subject/hypothesis of the manuscript or need modification? Yes, it is. 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript or need modification? Yes, it is. 3 Key Words. Do the key words reflect the focus of the manuscript? Yes, it is. 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes, it is. 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc) in adequate detail? 1) The intervention period is only two weeks, which is too short a time. 2) Whether the beverage has been approved for human use and whether its safety has been verified. 3) Please provide the batch number of the beverage. 4) The observational measures are too simple, too subjective (questionnaires on patients' self-perception may bias the results), and have no objective or quantitative basis. It would be fine if we had analytical data on the gut flora. 6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? No, it isn't. 7 Discussion. Does the manuscript discuss the findings adequately and



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appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? Yes, it is. 8 Illustrations and tables. Are the figures, diagrams, and tables sufficient, good quality and appropriately illustrative, with labeling of figures using arrows, asterisks, etc, and are the legends adequate and accurately reflective of the images/illustrations shown? Yes, it is. 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? Yes, it is. 10 Units. Does the manuscript meet the requirements of use of SI units? Yes, it is. 11 References. Does the manuscript appropriately cite the latest, important and authoritative references in the Introduction and Discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Yes, it is. 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? Yes, it is. 13 Research methods and reporting. Authors should have prepared their manuscripts according to BPG's standards for manuscript type and the appropriate topically-relevant category, as follows: (1) CARE Checklist (2013) - Case report; Not provide. (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; Not provide. (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; Not Applicable. (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; Not provide. and (5) The ARRIVE Guidelines -Basic study. Not provide. For (6) Letters to the Editor, the author(s) should have prepared the manuscript according to the appropriate research methods and reporting. Letters to the Editor will be critically evaluated and only letters with new important original or complementary information should be considered for publication. A Letter to the Editor



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that only recapitulates information published in the article(s) and states that more studies are needed is not acceptable. 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Not provide.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06730456

Position: Peer Reviewer

Academic degree: PhD

Professional title: Research Assistant Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-09-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-03 07:51

Reviewer performed review: 2023-10-03 10:01

Review time: 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

1.The components of the amino acid based medical food beverage in this study included should be described more specific.The paper should not just list the names of ingredients. And should specify whether the medical food beverage is self-made or purchased separately. 2.Both observation and control groups are necessary. The authors designed only one group during the conduct of this study. Further explanation is required. 3.This paper does not explain adequately that the amino acid based medical food beverage has a good efficacy on IBSD. Patients with IBSD are often associated with anxiety, depression, and other adverse emotions due to abnormal expression of inflammatory factors and VIP Levels. A key issue is the lack of above pharmacodynamic indicators. 4.The author may need additional experiments.Only IBS-SSS method is not enough , IBS-QOL and HAMD The can also be used to evaluate the function of the amino acid based medical food beverage. 5.Did the subject take any other medications in addition to the beverage? If so can it be clarified whether the beverage had a therapeutic effect or whether the other medication had a therapeutic effect, the author need to explain.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02536349

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: United States

Manuscript submission date: 2023-09-29

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-10-07 06:42

Reviewer performed review: 2023-10-07 20:25

Review time: 13 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

By means of the logic, methodology and use of indices this is a well-designed study. The title is compatible with the manuscript. However the duration, lack of placebo and different interference of IBS support and drugs (ie. rifaximin) make the approach debatable. Since the product (Enterade-trademark) is in a commercial status, the study had to be placebo controlled. In such a commercial product study such an observational, real-life data pattern may be questionable. Thus study had to include Calprotectin, anti tissue transglutaminase IgAi Total-IgA, anti-CdtB and anti-vinculin antibodies, differential diagnosis supported by upper and lower endoscopies and biopsies. Also, 2 weeks is not sufficient to conclude a beneficial effect. The follow-up period shouldn't be less than 12 weeks and preferably it may be 6 months. Drawing a result without a placebo controlled double blind randomised trial in such a study may not give a reliable conclusion. Despite those caveates, thank you for this high-level well-written manuscript.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00068348

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Surgeon

Reviewer's Country/Territory: Greece

Author's Country/Territory: United States

Manuscript submission date: 2023-09-29

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-10-07 22:15

Reviewer performed review: 2023-10-17 10:31

Review time: 9 Days and 12 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
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Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The article deals with a interesting issue which concerns a lot of patients with irritable bowel syndrome. The stud is well organized. The number of patients is relatively high. The parameters are well set up. The results support the primary hyypothesis. I believe the conclusion of the study provides a benefit for patients and doctors who are dealing with diarrhea issues due tto irritable bowel syndrome.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastrointestinal Pharmacology and Therapeutics*

Manuscript NO: 88566

Title: Effectiveness of an amino acid beverage formulation in diarrhea-predominant irritable bowel syndrome: A pragmatic real-world study

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06730456

Position: Peer Reviewer

Academic degree: PhD

Professional title: Research Assistant Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-09-29

Reviewer chosen by: Cong Lin

Reviewer accepted review: 2023-10-17 13:42

Reviewer performed review: 2023-10-17 13:49

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [**Y**] No

SPECIFIC COMMENTS TO AUTHORS

This article summarises the central studies conducted in IBD settings using non-PEG preparations by discussing their results. It is very meaningful.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 02536349

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: United States

Manuscript submission date: 2023-09-29

Reviewer chosen by: Cong Lin

Reviewer accepted review: 2023-10-18 16:07

Reviewer performed review: 2023-10-19 04:10

Review time: 12 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is a study on a commercial multi-ingredient amino acid based oral rehydration solution in IBS-D patients who were taken diagnosis by a wide range of multicenter sources. This manuscript may increase the awareness and importance of supportive diets besides classical treatment of IBS-D. Despite to caveates mentioned previously, a sentence expressing the inability to decide the main ingredient primarily responsible from the beneficial effect have to be added. Since this is somewhat a shotgun therapy, besides AAs , electrolytes and vitamines may ameliorate the QoL. Among ingredients, there are contradictory results of Zinc on IBS, beneficial or irritating which may ne the cause of side effects. Some omitted literature evaluating Enterade should also be discussed.