

Response to the reviewers for Gut-skin axis: emerging insights for gastroenterologists- a narrative review

Reviewer #1:

Specific Comments to Authors:

This review assessed the skin-gut axis from different aspects, including immune modulation, systemic inflammation, and gut microbiota dynamics. The authors explain the skin manifestations of gut disorders according to these aspects. They discuss an important issue on the role of medicines targeting the microbiota on the gut and skin manifestations. There are few queries about this review:

Introduction

This review looks like a narrative review, so add to the title "A narrative review"

NS: Thanks for the suggestion, we have changed the title as suggested.

Is there a similarity in the microbes species in the skin and gut? If there is no similarity then the assessment of GSA is based on the microbiota metabolites.

NS: Thanks for the comments. The microbiome of skin and gut are different. The interaction of gut and skin is based on multiple factors including but not limited to microbiota metabolites, immune and endocrine mechanism. The same has been mentioned in the section "understanding gut skin axis".

3. Dysbiosis is not restricted to the inflammatory bowel disease, but also in the irritable bowel disease (Gut dysfunction) and it is also associated with a flare up of acne rosacea. It will be more attractive to add a paragraph that GSA has a role in both functional and pathological gut disorders

NS: Thanks for the comments. We have now added the same and now mentioned in detail the effect of GSA on irritable bowel syndrome

The objective of this review is clear Understanding the Gut-Skin axis

Figure 1: It does not appear as a network and it is so brief. It requires more specifications and it will be nicely appeared as a network (because the term bidirectional is the hallmark of this review)

NS: Thanks for the comments. We have now modified this figure to show bidirectional network.

Add examples of dysbiosis metabolites that interfere with immunomodulation as a brief graph

NS: Thanks for the comments. We have created a table (Table 2) enlisting all key microbial metabolites which interfere with immunomodulation of GSA.

Mechanisms of Interaction

Is there a relation between a specific metabolite and specific skin lesion? P-cresol is associated with a

specific skin lesion? Add a brief sentence.

NS: Thanks for the comments. A specific skin lesion can be associated with multiple metabolites and the same has already been mentioned in the section “mechanism of interaction”

Clinical Implications for Gastroenterologists

It will be highly attractive if summarize the types of skin lesions with their diseases as a diagram. Please add the role of immunomodulation in each skin lesion as it appears with psoriasis “overlapping inflammatory pathways involving TNF- α , IL-23, IL-17, and IL-22”

NS: Thanks for the comments. The table 3 mentions all cytokines with their role in gi diseases as well as skin diseases.

Celiac disease and its associated skin conditions

1. Please clarify whether there is a significant difference in the skin manifestations between celiac diseases in children and adult type?

NS: Thanks for the comments. Yes there are few clinical differences in skin manifestations between skin manifestations of children and adults. We have now added this in the manuscript.

Microbiome and Skin disorders

No comments

Role of Pro/Pre-biotics in GSA

No comments.

It is so interesting.

Role of FMT in GSA

The subheading SLE, write it full term systemic lupus erythematosus

NS: We have made the correction.

Emerging Insights on Gut-Skin axis

Please, use italic font on typing bacterial species

NS: We have now typed all bacterial species in italic

References

1. Recheck references no. 60, 85

NS: Thanks for pointing this out, we have now corrected the references as per guidelines

2. About one-third of total references were published between 2020-2024. Please update the references to the accepted number

NS: Thanks for the comments. We have now edited the references as per guidelines

Reviewer #2:

Specific Comments to Authors:

This article comprehensively summarizes the bidirectional interaction between the gut and skin axis, and explores the pathogenesis and treatment of skin diseases from the perspective of the gut, which has certain clinical significance. However, there are also some minor issues in this article

1. Add some mechanism pictures for better understanding. Please supplement the role of light and vitamin D between the two.

NS: Thanks or the comments. We have now added a section on role of ultraviolet light, Vitamin D on gut. We have also added Figure 2 showing mechanism of GSA.

2 Editorial Office's comments

1) Science Editor:

1 Scientific quality: The authors submitted a review of the gut-skin axis.

(1) Classification: Grade A and Grade B;

(2) Summary of the Peer-Review Report: This article has certain clinical significance. However, the following problems still need to be solved.

Add some mechanism pictures for better understanding. Please supplement the role of light and vitamin D between the two.

NS: Thanks or the comments. We have now added a section on role of ultraviolet light, Vitamin D on gut. We have also added Figure 2 showing mechanism of GSA.

It will be more attractive to add a paragraph that GSA have a role in both functional and pathological gut disorders;

NS: Thanks for the comments. We have now added the same and now mentioned in detail the effect of GSA on irritable bowel syndrome.

Is there is a relation between a specific metabolite and specific skin lesion? and Please clarify whether there is a significant difference in the skin manifestations between celiac diseases in children and adults?

NS: Thanks for the comments. A specific skin lesion can be associated with multiple metabolites and the same has already been mentioned in the section "mechanism of interaction"

Manuscript Type: After verification, the manuscript type is "Review".

2 Specific comments

(1) Country/Territory of origin: India.

(2) The language classification is Grade A and Grade A. Please provide the latest language certificate after Return the Manuscript to Author for Revision. Please visit the following website for the professional English language editing companies that we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

NS: We have provided the language certificate.

(3) Manuscript Title:

The title should not start with 'The'.

Except for capitalization of the first word, all other words are represented in lowercase.

NS: Thanks for pointing this error. We have made the necessary correction.

(4) Please add "Author list".

NS: We have now added the author list.

Author names (unabbreviated) should be given as first name, middle name initial (with no period) and family (sur)name, and typed in bold with the first letter of each capitalized.

(5) Please add "Authors and institution(s)": Author names should be written out first (as first name, middle name initial (with no period) and family (sur)name) and typed in bold, followed by a comma and the complete name of the affiliated institution, city, province/state, postcode and country typed in non-bold. Examples for authors name and institutions are:

Neeraj Singla, Medical Gastroenterology, Fortis Hospitals, Ludhiana 141123, Punjab, India

NS: We have updated the same.

(6) Please add "Author contributions": The 'Author contributions' passage describes the specific contribution(s) made by each author. The author's names will be listed in the following format: full family (sur)name, followed by abbreviated first and middle names. For example, Bryan L Copple should be revised as Copple BL. A full multi-author example is: Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research study; Wang CL, Zou CC, Hong F and Wu XM performed the research.

NS: We have now added the author contribution.

(7) The "Key Words" does not meet the requirements:

The first letter of each keyword will be capitalized, and each keyword will be separated by a semicolon, with no terminal period. An example of correct formatting is: Non-alcoholic fatty liver disease; Alcoholic liver disease; Non-alcoholic steatohepatitis; Insulin resistance; Oxidative stress.

NS: We have corrected the same.

(8) Audio Core Tip. In order to attract readers to read the full-text article, we request that the first

author make an audio file describing the final core tip. This audio file will be published online, along with the article. The author can invite English language editing company to assist in resolving the language issues of Audio Core Tip.

NS: We have added the audio core tip

(9) Reference numbers in the main text.

The name of the author(s) of a reference is listed in the sentence, the reference number should be placed immediately after the author(s) of the reference. Example: Mandal et al[8] proposed that retractor aponeurosis disinsertion is the most likely cause of congenital low lid entropion.

NS: We have corrected the same.

(10) There are issues with the references:

To ensure the accuracy of the references, please use "Edit References by Auto-Analyser" (<https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx>) to edit the references of the manuscript.

NS: We have corrected the same.

(11) Figures.

Original figure documents. In the meantime, authors should provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor, and upload it to the file destination of "Image File" in the F6Publishing system.

NS: We have provided original figure documents as per requirement.

(12) Tables.

Tables must be presented in the order that they appear in the main text of the manuscript (numbered as 1, 2, 3, etc.).

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

NS: We have provided tables documents as per requirement.

(13) Please verify if all pictures (s) are original? If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published, and correctly indicate the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. *World J Gastroenterol* 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.

NS: We verify that all pictures are original.

3 Recommendation: Transfer to other BPG journals.

Language Quality: Grade A (Excellent)

Scientific Quality: Grade B (Very good)

2) Company Editor-in-Chief:

I recommend the manuscript to be published in the *World Journal of Gastrointestinal Pathophysiology*.

