



PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 62702

Title: Gut microbiota as a target for prevention and treatment of type 2 diabetes:
Mechanisms and dietary natural products

Reviewer's code: 05429012

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Jordan

Author's Country/Territory: China

Manuscript submission date: 2021-01-28

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-03-31 03:24

Reviewer performed review: 2021-04-07 04:59

Review time: 7 Days and 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 Grade E: Do not publish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 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
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



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SPECIFIC COMMENTS TO AUTHORS

Although the article is good, but blanks are left which makes barriers to follow the authors. The gut microbes look to play controversial roles, a matter that is good to be understood and further studied more than to give final images. I agree with the authors about the difficulties in targeting the study subject, but how these issues can be transferred into facts. diabetes has been known for more than 3500 years, and I think that it is a developmental disease. It is good if the author adds a new paragraph in the developmental aspects of diabetes in response to gut microbes. Regarding the figures, I do not know if the figures are produced by the authors or copied from secondary sources. the authors have to frankly answer this question, and if they are copied, is/are there any permission/s?



PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 62702

Title: Gut microbiota as a target for prevention and treatment of type 2 diabetes:
Mechanisms and dietary natural products

Reviewer's code: 05393454

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: India

Author's Country/Territory: China

Manuscript submission date: 2021-01-28

Reviewer chosen by: Jin-Lei Wang

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Review time: 8 Days and 21 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 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 checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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



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SPECIFIC COMMENTS TO AUTHORS

1. The English need improvement since there are some grammatical and syntax errors in the manuscript (For example, the words “Methanismsand” may be as “Mechanisms and” as “”; “” as “- in the title”; “overall” as “the overall”; “examination” as “the examination”; “in host” as “in the host”; “of Human” as “of the Human”; “host are” as “host is”; “expenditure were” as “expenditure was”; “than cause” as “than a cause”; “progression” as “the progression”; “have low” as “have a low”; “to high” as “to the high”; “to improvement” as “to the improvement”; “expression” as “the expression”; “in intestinal” as “in the intestinal”). The grammar mistakes which are not mentioned here also to be checked and corrected properly. 2. There are a few typing mistakes as well, and authors are advised to carefully proof-read the text (For example, the words “microbiotaas” may be as “microbiota as”; “(T1DM),gestational” as “(T1DM), gestational”; “(IDF),latent” as “(IDF), latent”; “maturity onset” as “maturity-onset”; “includestype” as “includes type”; “showsthat” as “shows that”; “inthis” as “in this”; “Thereis” as “There is”; “timethylamineN” as “time thylamine N”; “anddescribeshow” as “and describe show”; “canimprove” as “can improve”; “willrise” as “will rise”; “prevalenceof” as “prevalence of”; “causingmultiple” as “causing multiple”; “dysfunction,inflammatory” as “dysfunction, inflammatory”; “havestarted” as “have started”; “andprovidesignals” as “and provides signals”; “[22].Further” as “[22]. Further”; “haslower” as “has lower”; “tissue,pancreas” as “tissue, pancreas”; “glycemia regulation” as “glycemic regulation”; “multidimensional,including” as “multidimensional, including”; “oxidation,as” as “oxidation, as”; “[42] ,” as “[42],”; “Jockenet” as “Jocken et”; “andinsulin” as “and insulin”; “BCAAahave” as “BCAAs have”; “andmammalian” as “and mammalian”; “affecthost” as “affect host”; “causingenergy” as “causing energy”; “andinduces” as “and induces”; “andoriginates”



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as “and originates”; “oxidizesTMA” as “oxidizes TMA”; “TMAO.There” as “TMAO. There”; “shownthat” as “shown that”; “todecrease” as “to decrease”; “andincrease” as “and increase”; “promotesnormal” as “promotes normal”; “arestill” as “are still”; “leadingto” as “leading to”; “whichis” as “which is”; “humans,and” as “humans, and”; “bilesalhydrolyase” as “bile salt hydrolyase”; “millimolarconcentrations” as “millimolar concentrations”; “competesfor” as “competes for”; “regulatinglipid” as “regulating lipid”; “gutmicrobiota” as “gut microbiota”; “Thisemphasizes thatchanges inthe” as “This emphasizes that changes in the”; “intestine,FXR” as “intestine, FXR”; “host.The” as “host. The”; “abundanceof” as “abundance of”; “,increase” as “, increase”; “inplants” as “in plants”; “areinversely” as “are inversely”; “activityof” as “activity of”; “increasesabundance” as “increases abundance”; “decreasesthe” as “decreases the”; “improvingIR” as “improving IR”; “isrelated” as “is related”; “largeheterogeneous” as “large heterogeneous”; “toall” as “to all”; “arealso” as “are also”; “stress;inhibition” as “stress; inhibition”; “);promotion” as “); promotion”; “ofpolyphenols” as “of polyphenols”; “[125].Quercetin” as “[125]. Quercetin”; “hasa” as “has a”; “andprotease” as “and protease”; “thealkaloids” as “the alkaloids”; “chinensisFranch” as “chinensis Franch”; “thegut” as “the gut”; “shownthat” as “shown that”; “ofthe” as “of the”; “feces[” as “feces [”; “ofBCAA” as “of BCAA”; “ofthe” as “of the” ; “ofgut” as “of gut”; “products,such” as “products, such”; “hostmetabolism” as “host metabolism”; “Thisis importantfor” as “This is important for”; “onhostmetabolism” as “on host metabolism”; “Ofgut” as “Ofgut”). The typos not mentioned here also to be checked and corrected properly. 3. The keywords that are not in the title should also be included in the other parts of the manuscript. The keywords should assist computer searches to find your specific article. 4. The databases or search engines used (like PubMed, ScienceDirect, Google scholar etc.) for collection of this information with the keywords (in the text) used should be mentioned. 5. Check the abbreviations throughout the manuscript and



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introduce the abbreviation when the full word appears the first time in the text and then use only the abbreviation. And it should be in both abstract as well as in the remaining part of the manuscript.



PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 62702

Title: Gut microbiota as a target for prevention and treatment of type 2 diabetes:
Mechanisms and dietary natural products

Reviewer's code: 02951605

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Czech Republic

Author's Country/Territory: China

Manuscript submission date: 2021-01-28

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-03-31 05:52

Reviewer performed review: 2021-04-10 21:09

Review time: 10 Days and 15 Hours

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
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 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



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SPECIFIC COMMENTS TO AUTHORS

1) Abstract - "Diabetes mellitus (DM) is one of the biggest public health concerns worldwide and includes type 1, type 2, gestational, and other rare forms." - avoid referring to other types of diabetes when the review should be centered on T2DM 2) Abstract - a large part of the abstract is rather introductory and provides very limited indices for the potential reader, which would motivate he/she to open the full-text. Rewrite the abstract in a way that it is more focused and avoids the textbook-like phrases and superficially covered facts. 3) Abstract - check the manuscript for the presence of typos, like "timethylamine" 4) Core tip - "However, because the composition of natural products is so complex that gut microbiota may also influence the metabolism of natural product in host, further studies should focus on the metabolism of natural products and their bioactive components by gut microbiota" - it is unclear why it would be surprising that the microbiota is affected by the consumed food. Specify whatever is related to T2DM. 5) Introduction - "which is rising more rapidly in middle- and low-income countries[1,2]" - this could be true but check where the diabetes prevalence is already high 6) Introduction - "According to the classification of the International Diabetes Federation (IDF) in 1997," - refer to the most recent ADA guidelines published in Diabetes Care instead of this several decades old source. 7) Alternation... - "indicating that these bacteria were more specific to T2DM than obesity was[22]." - ref. #22 is a review. Replace it with primary reference(s). Double-check, whether the respective sentence tells what you aimed to tell - the fact that the bacteria segregated more with glucose levels than with obesity does not mean that obesity was not specific to T2DM. 8) Metabolites... - "mouse⁷⁰ and bovine⁷¹ cells" - the meaning of the numbers is unclear 9) Metabolites... - "Peptide YY (PYY) is released into the circulation" - the respective subchapter is about SFAs, so avoid starting the para with



the peptide YY. It is necessary to make the text fluent and to guide the reader through the topics covered. 10) Metabolites... - "inulin propionate ester supplementation at 10 g/d when compared with 10 g/d inulin alone" - do you mean that the mice (20g-weighting animals) were fed with 10g inulin daily? That is irrelevant. The mouse typically eats 3-5 g of food per day. 11) Metabolites - "Hattori et al showed that acetate administrated orally, in comparison to distilled water, increased energy expenditure and lipid oxidation[44]. Similar to the above results, acetate (5.2 mg/kg)" - when claiming that something was administered orally, always make sure how exactly was it administered, whether in form of some solution, capsules, gavage, etc. By the way, which acetate? There are many acetates... 12) Branched... - "Inflammatory factor signaling pathways, including the nuclear factor (NF)- κ B pathway and mammalian target of rapamycin complex 1 (mTORC1), might be candidate therapeutic targets" - please specify why do you consider mTORC1 to be an "inflammatory factor signaling pathway" in a context of the gut environment. mTOR is a major nutrient sensing pathway and is important across multiple cell types. 13) Fig. 2 - the bottom half of the figure needs to be improved in order to avoid the current (likely unnoticed) interpretation that the discussed pathways are affected in blood vessels 14) Metabolic endotoxemia - "The amount of Bifidobacterium is significantly and negatively correlated with high portal plasma levels of LPS in HFD-induced models[86]. However, by using a broad-spectrum antibiotic (ampicillin and neomycin), metabolic endotoxemia and cecal content of LPS in ob/ob mice are dramatically reduced, and then the glucose intolerance, inflammation and body weight are also improved[81]." - these two sentences should not be interconnected, as the two mentioned antibiotics are not selective for Bifidobacterium and therefore the causative link cannot be established with this argument. 15) Interactions... - "Clinical data prove that BAs induce metabolic disorders, such as disorders of lipid, glucose and energy metabolism, as well as



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inflammatory cytokine generation, which are closely related to T2DM[100].” – this is not true. The dysregulation of bile acid homeostasis could cause that but do not attribute this effect to a simple presence of bile acids. 16) Table 1 – “Increasing the ratio of Bacteroidetes and Firmicutes in intestine” – should “and” be replaced with “to”? 17) Table 1 – check, whether all the claims are correct. For example, the claim “abundance of Bacteroidetes, Prevotella and Deltaproteobacteria” does not make sense because Prevotella is part of Bacteroidetes. 18) Table 1 – references should be in the same format as in the rest of the text. 19) Many recent references point to journals with questionable peer-review practices, like Theranostics. Please make sure that all the claims are supported by trusted references. 20) The formatting of references is inconsistent. Check, for example, the presence/absence of capital letters in “Nature reviews Endocrinology” 21) The current figures are fine but there is no figure, which would focus on the bacteria diversity and changes in bacteria diversity with respect to diabetes 22) Polyphenols – “Resveratrol attenuates HFD-induced NASH ameliorates the intestinal barrier dysfunction and inflammation in rats[125].” – check the dose used, it was far above the “safe” dose for humans. Check also other compounds mentioned in this manuscript for the same issue.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Diabetes

Manuscript NO: 62702

Title: Gut microbiota as a target for prevention and treatment of type 2 diabetes:
Mechanisms and dietary natural products

Reviewer's code: 02951605

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Czech Republic

Author's Country/Territory: China

Manuscript submission date: 2021-01-28

Reviewer chosen by: Chen-Chen Gao

Reviewer accepted review: 2021-05-11 09:31

Reviewer performed review: 2021-05-11 10:36

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
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 checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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



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The provided comments were reflected to a sufficient extent. - Language check is necessary, there is a typo already in the manuscript title. - There are still unnecessary parts of the text left. These include, for example: "According to Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes in 2020, there are three main types of DM, including type 1 DM (T1DM), type 2 DM (T2DM) and gestational DM (GDM). However, there are some other types of diabetes, such as autoimmune latent diabetes in adults (LADA), pancreatic diabetes, and maturity onset diabetes of the young (MODY)1-3[3]." - these textbook-like facts can easily be deleted and the manuscript trimmed accordingly. - Many of the relevant recent references are uncited. These include, for example, Acta Diabetol. 2021 May 10. doi: 10.1007/s00592-021-01727-5. Diabetes Metab Syndr Obes. 2021 Apr 28;14:1855-1869. Clin Transl Med. 2021 Apr;11(4):e326. PeerJ. 2021 Apr 1;9:e11128. Gut. 2021 Mar 30;gutjnl-2020-323617. and many others. - There is no method disclosed concerning how the reviewed papers were selected. However, given that the recent papers are nearly completely absent, it is necessary to check the major abstract databases for relevant papers, read through the full-texts and extract relevant information into this review. This could be a time-demanding task, as the review would be virtually rewritten in many of its parts. - Many concepts are developed here based on old models. For example, the authors state that "Transplantation of microbiota from genetically obese to germ-free mice caused a significant weight increase compared with germ-free mice that were transplanted with microbiota from thin mice[19]." However, the authors completely avoid informing the reader that fecal transplantation was applied in numerous studies targeting obesity in humans. Many other such examples exist through the manuscript.