

Dear Editor,

We are very pleased to accept your kind invitation to write this review, and very grateful for giving us this chance. We thank and appreciate the Editor's constructive comments and suggestions, which greatly helped us to improve the manuscript. In this context, we are open to do any further suggestions to enhance the quality of this work.

In the light of your comments, we revised our manuscript as follows:

#1) Editor and Reviewers raised points

#1.1) The title cannot summarize the entire content

Reply: We thank the editor for the deep understanding of our work, and we totally agree. Per editor and reviewer's suggestion, the title will be changed to "Antidiabetics and antimicrobials: harmony of mutual interplay"

#1.2) The format needs to be adjusted and there are typos

Reply: We thank editor your interest in our work, we followed the journal format and reference style which is indicated in the author guidelines. The manuscript has been revised carefully for typos and all mistakes were corrected.

#1.3) The questions raised by the reviewers should be answered

Reply: We replied all the points raised by the reviewers and make any needed modifications or corrections as indicated in the revised manuscript. Please find the response to the reviewers.

#1.4) ABBREVIATIONS

Reply: According the provided instructions about abbreviations, we declared all abbreviations in the text and in figures.

#2) The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement.

Reply: The needed formats were downloaded from journal website, signed and will uploaded with revised manuscript.

#3) Editor raised issues

#3.1) I found no "Author contribution" section. Please provide the author contributions

Reply: We add Author contribution in the main text.

#3.2) I found no "Core tip" section. Please add

Reply: We add Core tip in the main text.

#3.3) I found the authors did not provide the original figures. Please provide the Figures cited in the original manuscript in the form of PPT. All text can be edited, including A, B, arrows, etc. With respect to the reference to the Figure, determine if it is the original Figure, if not, please provide the source of the picture and the proof that the Figure has been authorized by the previous publisher or copyright owner to allow it to be redistributed.

Reply: We Declare that the figures in this manuscript are originally designed and invented by us. We confirm that we never quote or modify these figures from any other sources. The original, editable figures are uploaded with the revised manuscript.

#3.4) Please write the “Conclusion” section at the end of the main text.

Reply: We add Conclusion in the main text.

We hope the editor could accept our modifications

We believe that our revised manuscript reaches the criteria to accept for publication.

Finally, we really thank the editor for kind and critical comments

For Reviewer #1

We appreciate the reviewer for your valuable and constructive comments and suggestions, which greatly helped us to improve the manuscript. In the light of your comments, we revised our manuscript as follows:

#1) The title cannot summarize the whole content of the review, i.e., the interplay between diabetes, infection and immunity.

Reply: We thank the reviewer for his deep understanding of our work, and we totally agree. The title will be changed to "Antidiabetics and antimicrobials: harmony of mutual interplay"

#2) The font size in Fig. 1 is too small to read, which could be condensed to make the key points larger.

Reply: Per reviewer suggestion, we modified the font sized to be readable.

#3) English abbreviations should be introduced for the first time with the full name and then followed by direct use of abbreviations.

Reply: We thank the reviewer for your interest in our work. Per reviewer suggestion, we defined the abbreviations at their first use.

#4) Page or line should be numbered. Typos for example: a) Fig. 2: “Nf-KB” should be “NF-κB”. b) Page 13, line 6: “reduced glutathiones” should be “glutathione”. c) Page 28, line 18: “repoting” should be “reporting”.

Reply: We thank the reviewer for your comment. Accordingly, we corrected all mistakes.

We hope the reviewer could accept our modifications

We believe that our revised manuscript reaches the criteria to accept for publication.

Finally, we really thank the reviewer for kind and critical comments.

For Reviewer #2

We appreciate the reviewer for your valuable and constructive comments and suggestions, which greatly helped us to improve the manuscript. In the light of your comments, we revised our manuscript as follows:

#1) The figures need overhaul, the texts placement and the designs were poor

Reply: We thank the reviewer for his interest in our work, fine adjustments were applied to the figures to improve the fonts, placement of the texts and the overall design of the figures. We appreciate the reviewer's opinion and we are open to do any further suggestions to enhance the quality of this work.

#2) The manuscript has to be more focused according to its title, not too much discuss irrelevant topic, despite it's associated.

Reply: We thank the reviewer for your deep understanding, and we totally agree. The title will be changed to "Antidiabetics and antimicrobials: harmony of mutual interplay" to describe the manuscript content.

We hope the reviewer could accept our Explanation

We believe that our revised manuscript reaches the criteria to accept for publication.

Finally, we really thank the reviewer for kind and critical comments.

For Reviewer #3

We appreciate the reviewer for your valuable and constructive comments and suggestions, which greatly helped us to improve the manuscript. In the light of your comments, we revised our manuscript as follows:

#1) Before the COVID-19 pandemic 650 million adults (13% of the world's adult population) were obese. Kelly et al. (2008) estimated that 19.7% of the world's population will be obese by the year of 2030. In addition, momentarily due to COVID-19 pandemic and quarantine measures, it is highly certain that global burden of obesity will escalate even more. Since diabetes type 2 is one of the most prevalent complications of obesity; if I were you I would take into account latter (and provide a short note/comment) in introduction paragraph were you give projection regarding diabetes rates (especially since the reference 1 was before pandemic situation and secular trends have potentially changed now).

Reply: We thank the reviewer for your deep understanding and totally agree with the reviewer's invaluable suggestion. According to reviewer's fruitful comment, we added these lines (with references) to the introduction as follows (lines 48-57):

Before the COVID-19 pandemic 650 million adults (13% of the world's adult population) were obese and it was estimated that 19.7% of the world's population will be obese by the year of 2030 [2]. The Covid-19 pandemic has been associated with increased risk of obesity and associated health hazards mainly diabetes. The global application of quarantine requirements forced billions of people into a new life style of isolation where people are forced to spend more time indoors with minimum physical activities and limited contact with others. The quarantine related frustration pushed people to consume larger amounts of high sugar foods which is reflected as higher incidence of obesity [3, 4]. Moreover, many studies have outlined the role of obesity and diabetes as important risk factors in COVID-19 infections [5, 6].

#2) When dividing diabetes to types, I would may be also add that it depends on pathophysiological cascade, besides age of onset and the need for external insulin (especially since insulin is also a common therapeutic measure among T2DM patients also).

Reply: We thank the reviewer for your deep understanding and totally agree with the reviewer's comment. Need for external insulin should not be used to discriminate between the diabetes types, as insulin is needed in both. So, we add sentence in line 58-59:

Diabetes is commonly divided into two major categories depending on the age of onset and the pathophysiological cascade of events giving rise to diabetes.

And then we declared that both types need insulin either from beginning of T1DM or in later stages in T2DM, as described in lines 60-66.

#2) Regarding your comment on IL-1B and TNF inhibitors, I would paraphrase or remove that statement, since it is not routinely prescribed at the moment

Reply: Per reviewer suggestion, we removed this statement from the text (line 86).

We hope the reviewer could accept our modifications

We believe that our revised manuscript reaches the criteria to accept for publication.

Finally, we really thank the reviewer for kind and critical comments