



UNIVERSITA' degli STUDI di CATANZARO "MAGNA GRÆCIA"

DIPARTIMENTO DI SCIENZE DELLA SALUTE

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Catanzaro, 8 March 2017

Ya-Juan Ma

Scientific Editor

World Journal of Gastroenterology

Dear Dr. Ya-Juan Ma,

Re: MS 00033405 "Potential role of nutraceutical compounds in inflammatory bowel disease" Manuscript Type Editorial – Revision 1 by Tiziana Larussa et al.

Thank you for your mail of 27 February 2017 and for giving us the opportunity to modify and improve the above manuscript. We took on board the comments raised by the reviewers and revised the manuscript accordingly.

Enclosed please find the revised manuscript as well as a point-by-point reply to the reviewer's comments.

Again thank you for your consideration and for giving us the opportunity of learning from the reviewers' comments.

We would be grateful if the manuscript could now be considered for publication in the ***World Journal of Gastroenterology***.

- 1) English language has been revised by a native English Speaker Colleague, as reported in the Acknowledgment Section. All the manuscript was revised for typing errors and English grammar, as highlighted in red
- 2) Corresponding address has been revised
- 3) Authors contributions have been added
- 4) Audio Core Tip has been provided
- 5) Details on the currently accepted classification of nutraceuticals have been provided (see page 4, lane 10-14)
- 6) As requested, the purpose of the manuscript has been clarified in the new version of the manuscript, in the Introduction section (see page 5, lane 1-4). We underlined the aim to discuss only nutraceutical compounds evaluated in human IBD trials.
- 7) As requested, comments both on the value of flavonoids (see page 7, lane 27-31; ref. 47) and other flavonoids beside anthocyanidins (see page 8, lane 9-11; ref.50) have been added. References' list has been modified as appropriate
- 8) Page 11, lane 4: undercarboxylated has been corrected with undecarboxylated
- 9) Page 11, lane 7: BMD stands for bone mineral density. Thank you for noticing the lack of explanation of the acronym
- 10) Format of references' numbers in Table 1 has been revised
- 11) Figures have been modified as requested
- 12) Acknowledgment Section has been added

Authors replay to the reviewers' comments

Reviewed by 02529456

Authors present interesting data on nutritional inputs in IBD. Comments; 1. a restructuring of the paper is needed, authors should perform a systematic review, rather than a selected presentation of the facts 2. Authors should clearly present search strategy and search terms, paper selection flowchart, which papers were included, which not, and why 3. present all papers in depth as a table which were included and rewrite discussion/conclusions accordingly

Response:

We have been invited to contribute with an Editorial and not with a Systematic Review. Consequently, the manuscript has been structured with the aim to describe the more common nutraceutical compounds used in IBD and to comment on recent findings for their possible applications in humans. The beneficial effects of the most investigated nutraceuticals compounds in IBD human setting are presented and discussed, highlighting the current available clinical trials' results. We focused our attention only towards studies involving human subjects, as stated in the manuscript's introduction and often repeated throughout the paper. A table presenting the available clinical trials using probiotics/prebiotics has been presented (see Table 1), but for the other paragraphs a picture describing the topic has been found more suitable, since cited papers were few.

Reviewed by 00049331

The Author reviewed the potential role of more common nutraceutical compounds in inflammatory bowel disease in this article. We know that treatment of IBD includes anti-inflammatory, immunosuppressive and immunomodulatory medication. However, the potential role of diet in IBD has been described in the literature. Nutraceuticals are food or part of food that provides medical or health benefits. Nutraceuticals can be grouped into three broad categories: 1. Substances with established nutritional functions, such as vitamins, minerals, amino acids and fatty acids, also defined nutrients. 2. Herbs or botanical products as concentrates and extracts, often called herbals. 3. Reagents derived from other sources (e.g. pyruvate, chondroitin sulphate, steroid hormone precursors) serving specific functions, such as sports nutrition, weight-loss supplements and meal replacements, also indicated as dietary supplements. These three categories are shown in figure 1. Nevertheless, author mentioned four subtitles "Probiotics and Prebiotics, Phytochemicals, Dietary lipids and fat-soluble vitamins, Dietary peptides and amino acids". These subtitles should be more ascertaining as listed under nutraceutical sub-categories (nutrients, herbals or dietary supplements). Which subtitles should be under placed which sub-category? After explanation, this paper is acceptable.

Response:

The three broad categories of Nutraceutical compounds, as described in the Figure 1, include: Nutrients, Herbals and Dietary supplements. However, this is only one of the possible classification of nutraceutical compounds and do not represent an official statement. For example, they can be classified on the basis of their natural sources, or according their pharmacological conditions, as well as chemical constitution of the products

and so on. Since our aim was to describe the most common nutraceutical compounds experienced in the context of human IBD, we did not present and discuss data deriving from in vitro or animal studies. Therefore, our focus has been restricted on the agents more representative in human IBD setting, regardless their placing in one of the possible categories above mentioned. The reported classification has a purely descriptive role and did not drive our search, nor is representative for the agents heading each of the four subtitles (e.g., Probiotics did not belong to any of the three categories mentioned in the cited classification, because as already mentioned this is just one of the possible classifications, but can be listed as a category of its own when considering a classification of nutraceuticals based on food sources - see ref. 11). This has been clarified in the new version of the manuscript (Introduction section, page 4, lane 10-14 and page 5, lane 1-4).

Reviewed by 02438889

This is a nice report on the role of nutraceuticals and their definition in patients with IBD. Lots of literature exists on the conventional therapy of IBD but little is known about the equally important therapy with compounds based on food and plant products. To improve the clinical results of treatment for IBD patients this novel approach needs to be implemented when making therapeutic decisions. However the active chemical compounds need to be tested similar to that of drug applications using pharmaceutical deliveries of these substances. Please note when discussing phytochemicals add: "Beside anthocyanidins other flavonoids exhibit nutritional values and their mode of action have been documented which includes their efficacy-Hoensch et al 2015, Clinical Nutrition Experimental and Langhorst et al 2013, Aliment Pharmacol Ther". There are 2 small mistakes on page 10: serum undecarboxylated not underdecarboxylated and low BMI not BMD.

Response:

Comments on both the value of flavonoids (see page 7, lane 27-31; ref. 47) and other flavonoids beside anthocyanidins (see page 8, lane 9-11; ref.50) have been added. References' list has been modified as appropriate.

Page 11, lane 4: undercarboxylated has been corrected with undecarboxylated.

Page 11, lane 7: BMD stands for bone mineral density. Thank you for noticing the lack of explanation of the acronym.

We look forward to hearing from you at your earliest convenience

Yours sincerely
Francesco Luzza

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