



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54470

Title: Potential of the ellagic acid-derived gut microbiota metabolite – Urolithin A in gastrointestinal protection

Reviewer's code: 03478404

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Romania

Author's Country/Territory: Poland

Manuscript submission date: 2020-01-31

Reviewer chosen by: Ruo-Yu Ma

Reviewer accepted review: 2020-02-26 16:06

Reviewer performed review: 2020-02-29 10:04

Review time: 2 Days and 17 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 Grade E: Do not publish
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input 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

The manuscript titled „Potential of the ellagic acid-derived gut microbiota metabolite - Urolithin A in gastrointestinal protection” represents a review of the all available to date studies in vitro, in animal models, as well as in humans. Accuracy of the data is much appreciated. The review is written in an elegant manner, easily to be followed. English language is of high quality. The authors highlight the chemopreventive and anti-inflammatory effects of Urolithin A (UA), with health benefits. The structure of the manuscript is well chosen, starting with the Introduction and then analyzing effects on colorectal cancer and inflammatory diseases, as well as on liver and pancreatic cancer and Barrett esophagus. 1. “Introduction” explains correctly the process of producing urolithins, and contains description of metabotypes and gut bacteria involved in urolithin A production (the type of urolithins associated with health benefits). Purpose is well stated: presenting the evidence of in vitro, in vivo and clinical studies showing the potential of Urolithin A in gastrointestinal protection, as well as of suggested mechanisms by which Urolithin A can protect against cancer and inflammatory diseases of the digestive tract. 2. The paragraph “Intestine” describes the effects against inflammatory bowel disease and colorectal cancer. A. Colorectal cancer: most chemopreventive effects are shown in „in vitro” research. Although there are numerous in vitro studies supporting UA as a CRC chemopreventive agent, there is a lack of clinical evidence in this area. Results of these studies are nicely summarized in Table 1. There is only one clinical study, showing inhibition of expression of several CRC-related genes in cancerous colon tissues, after consumption of an ET-containing pomegranate extract, but this effect is not associated with the Urolithin A level in the tissue. B. Inflammatory bowel disease: UA at a concentration that is achieved in the colon through the diet, may possess anti-inflammatory effects, including through modulating gut



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microbiota, activities against pathogens (like *Yersinia enterocolitica*) and enhancing gut barrier functions. Existing studies are performed “in vitro” and on animal models. Anti-inflammatory effects are synthesized in Table 2, of very good quality. 3. Chemopreventive effects on liver cancer are demonstrated only a few studies and one study on pancreas cancer; studies were performed in vitro and on animal models. There has been only 1 study (phase I) in humans with Barrett esophagus. Results of all these studies are presented clearly in Table 3. All data in this review are supported by correct references, including the most recent ones. Conclusion is adequate. Since Ellagitannins (precursors of Urolithin A) are found mainly in pomegranate, berries, and nuts, supplementation with these foods seems promising, although more research is required, especially in humans. Only two minor deficiencies: 1. Short (running) title is missing. 2. Copyright License Agreement is missing.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54470

Title: Potential of the ellagic acid-derived gut microbiota metabolite – Urolithin A in gastrointestinal protection

Reviewer's code: 01434943

Position: Editorial Board

Academic degree: PhD, BSc, RCPA

Professional title: Professor

Reviewer's Country/Territory: Australia

Author's Country/Territory: Poland

Manuscript submission date: 2020-01-31

Reviewer chosen by: Ruo-Yu Ma

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Review time: 2 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
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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SPECIFIC COMMENTS TO AUTHORS

This is a timely review concerning bioactive compounds, specifically Urolithin A, sourced from certain plants including pomegranates and berries. The overall structure, logical progression and scientific content are very good. English grammar requires attention throughout, especially the use of singulars vs plurals. The review is also a little verbose and would benefit from a more concise writing style. The Discussion would further benefit from a broader discussion of plant-sourced tannins and anthocyanidins in the sections on IBD and colorectal cancer (see studies on grape seed extract by Cheah et al).