Author's response to reviews

Title: Effects of olive oil and its minor phenolic constituents on obesity-induced cardiac metabolic changes

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Dr. Demitrakis Kavallierou  
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Effects of olive oil and its minor phenolic constituents on obesity-induced cardiac disease.  

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Dear Dr Kavallierou:  

Thank you for the e-mail dated June 21, 2010. The reviewers’ suggestions were of fundamental importance for the data interpretation, thank you very much.  

In attention to the recommendations, enclosed is a revised manuscript which has all the corrections indicated by the reviewers. I am including a numbered list indicating how I have dealt with each of the points raised by the reviewers.  

In attention to the Referee #1  

- “Raise the word – disease – from the title of the article”  

The Title of the article was changed to: Effects of olive oil and its minor phenolic constituents on obesity-induced cardiac metabolic changes.  

- “The authors need to specify why have been only male rats”  

The new version explains the choice for male rats: Methods - Obesity induction and experimental procedure- Page 4 (Lines 6 and 7).  

In attention to the Referee #2:  

1. “It is not clear how and what concentration the olive oil and phenolic compounds were administered. The treatments were given by gavage twice a week, but the dose was given per day”  

This was explained – Methods – Page 5 (Paragraph 1). The dose was given per day and this dose was given twice a week, during 3 weeks (21 days of treatments). New references were included on this issue.
2. “The modality of providing the compounds is neither chronic nor acute. Consequently, it would be necessary to monitor the concentration in plasma and urine”

The revised manuscript has explanation for the importance to determine the long term and low-dose intake of the compounds: Discussion – Page 7 – Paragraph 2 (Lines 4 – 5), and Methods – Page 5 (Paragraph 1): The olive oil administration was the adopted dose according to human olive oil consumption, and considered that the average consumption of olive oil in humans is 4% of the diet, twice a week. New references were included on this issue.

3. “Since the polyphenol content and composition can be extremely various in different extra virgin olive oils, information should be given about the amount of total polyphenols in the EVOO used for the study.”

The revised version includes the results of oleuropein and cafeic acid determinations in the EVOO used for the study: Methods - Page 5 (Paragraph 1). New references were included on this issue.

4. “The Result section did not offer a clear understanding of the data obtained”

The Result Section was changed to clear understanding of the data (Pages 6 and 7). In attention to the others Referees we deleted values of OHADH and CS from the Tables 4 and 5, and showed these determinations in Figs 1 and 2 (Page 20). The original Fig 1 was also deleted and the findings cited in the text (Page 8 – Paragraph 3 – Lines 1 and 2).

5. “The Discussion is in several parts quite speculative, and often the statements are unconvincing In particular, the discussion and interpretation of data on oxidative stress”

The Discussion was rewritten (Pages 7 – 10). The interpretation of data on oxidative stress was changed (Page 10 – Paragraphs 1 and 2). New references were included.

6. “Finally, should be discussed the significant differences found among the effects of olive oil, oleuropein and cafeic acid treatments.)”

The revised version discussed the differences among the effects of the treatments (Discussion, Pages 7 – 10), mainly on metabolic enzymes in cardiac tissue – (Pages 9, Paragraph 3: Curiously…).

In attention to the Referee #3:

1. “1st paragraph: In the 2nd sentence, the statement below should be removed”
   In the revised version the sentence in the first paragraph was deleted. New references were included on this issue Page 3 (Line 3).

2. “2nd paragraph, atherosclerosis should be corrected as atherosclerotic”
   This alteration was made in the revised version.
3. “According to which criteria were the doses of oleuropein and cafeic acid chose?”
   This was explained – Methods – Page 5 (Paragraph 1). New references were included on this issue.

In attention to the Referee #4:

**Major Comments**

- “The authors did not evaluated cardiac disease as an end point in the rats. They examined the effects of olive oil and some phenolic compounds on several parameters related with cardiac metabolism. Thus, this issue must be changed in the title, objective, hypothesis and conclusions”

  The revised version was changed, the cardiac disease was substituted for **metabolic changes** at the title, abstract, objective, hypothesis and conclusions.

- “The Discussion is too long and highly speculative”

  The **Discussion** was rewritten (Pages 7 – 10). The interpretation of data on oxidative stress was changed (Page 10 – Paragraphs 1 and 2). New references were included.

- “The Introduction leads to misinterpretations”

  The **Introduction** was altered and reduced (Page 3). Terms as lipid oxidation were changed to fat oxidation in the manuscript. New references were included.

**Minor Comments**

- “Abstract: Provide the number of days in which the rats were provided with olive oil and phenolic supplementation. The sentence concerning the application of polyphenols in food systems is too speculative and it is not a conclusion from the data of the study. The same occur in the Conclusions at the end of the Discussion”

  The revised version was changed. **Abstract (Page 2)**, and **Discussion (Pages 10 – 11)**.

- “Introduction. First paragraph the sentence : but whether ….The fact that olive oil minor constituents have beneficial risk factors for cardiovascular disease in humans is well established ”

  In the revised version the sentence in the first paragraph was deleted. The cited references were included - **Page 3 (Line 3)**.

- “Methods: Morphometric and biochemical determinations. First line 44 or 42 days?”

  The **Methods** were corrected. The determinations were made at 42 days of the experimental study (21 days of diet and plus 21 days of olive oil and phenolic compounds administration).
• “Results: The term Cardiac determinations must be substituted by Morphometric and biochemical determinations in the heart”

The term was substituted. Results – (Page 7).

• “Discussion. As has been referred to before it is too long and speculative”.

The Discussion was rewritten (Pages 7 – 10). New references were included. The observations on carbohydrate oxidation were changed (Page 8, Paragraph 2).

• Table 1. The fact that the data are from after 21 days of standard and hypercaloric diet must be referred in the title”

The Table 1 included the time of standard and hypercaloric consumption (Page 15).

• Tables 2 and 3. Why are no there data measurements of carbohydrate oxidation?’

The amount of carbohydrate oxidation was too low to be determined. As previously made (Seiva et al., Growth Horm & IGF Res, 2009;18:275-283) - The term not detected was mentioned – Tables 2 and 3 (Pages 16 and 17).

• Table 5. Can be substituted by a Figure representing changes in OHADH”

The new version included Fig. 1 representing changes in OHADH and Fig. 2 representing changes in CS. The Table 5 included oxidative stress parameters, in accordance with the others Referees.

• Figures 1 and 2. They are not necessary”

These original Figures were deleted. The lack of differences in the evaluated parameters were referred in the text (Page 8 – Paragraph 3 – Lines 1 and 2).

I sincerely hope that all alterations have been made for to consider the Reviewer’s corrections, and if the paper needs others alterations, I should change being so informed.

Thank you very much in advance.
Looking forward to reading from you.

Yours sincerely
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