

Format for ANSWERING REVIEWERS



March 24, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8799-review.doc).

Title: Antioxidants, inflammation and cardiovascular disease

Author: Harald Mangge, Kathrin Becker, Fuchs Dietmar, Johanna M. Gostner

Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 8799

The manuscript has been improved according to the suggestions of reviewers:

Reviewer 1 (02445965)

The review manuscript by Mangge et al., describes the aspects of antioxidants and inflammation on cardiovascular disease. The manuscript is thorough and mostly complete and outlines the potential factors that influence cardiovascular disease. This is timely and important. Two comments that this review would like at least addressed by the authors.

1) What about a short description of the inflammasome complex which has recently been of interest in atherosclerosis?

A description of the inflammasome complex has been added at the end of the section "role of lipoproteins in atherosclerosis".

2) Also, some mention about the conversion of macrophages between M0/M1/M2 would be appropriate.

The impact of different macrophage phenotypes is now discussed in section "oxidative stress and immune activation".

Reviewer 2 (02456031)

This is an interesting review discussing the evidence about the mechanism of atherogenesis, with special regards to the inflammatory and oxidative stress theory. It also tries to summarize current evidence on the effects of possible interventions with antioxidants. In general, the review lacks of a link with clinical practice and it should benefit from some more practical conclusions for the physician. Figures and Tables should be added to help the reader to understand this complex topic.

Introduction. Please, briefly declare the objective of this review.

The object of this review is now mentioned in the introduction part.

Main features of atherogenesis. It would be helpful for the reader to add a table or a diagram

summarizing the main pathogenetic aspects of atherogenesis. This would be useful particularly for the section "Oxidative stress", which is presently rather difficult to read. You can also expand and detail Figure 1, or link new Figures to Figure 1. Page 6.

The section "Oxidative stress" has been divided into "Oxidative stress and immune activation" and "Role of lipoproteins in atherosclerosis" for a better understanding.

Citation Valko et al., 2007. Please replace with appropriate reference number (25). This mistake repeats throughout the text for other citations. Please, revise.

References were corrected.

Neopterin formation. Please add a table summarizing the current evidence (and strength) of neopterin as an independent marker of CVD, as described in the text. This could also be applied to the subsequent sections, discussing the importance of other markers.

A table has been introduced that summarizes the current evidence of neopterin as an independent marker of CVD.

"Antioxidant in CVD therapy". A table summarizing pros and cons of various approaches (vitamin E, statins, others?) and relative strength of evidence might be very helpful in practical terms and could help to support current conclusions.

The conclusion section has been extensively revised.

Several correction regarding language, grammar and typesetting were made.

Thank you again for publishing our manuscript in the *World Journal of Cardiology*.

Sincerely yours,
Dietmar Fuchs

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