



SDI Review Form 1.6

Journal Name:	Ophthalmology Research: An international Journal
Manuscript Number:	2013_OR_5926
Title of the Manuscript:	Effects of micronutrients on serum antioxidant status of glaucoma patients: a randomized, placebo-controlled, double-masked pilot study
Type of the Article	Research Paper

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments X	1- The dose and period of antioxidant supplementation shall be mentioned much earlier in the manuscript (e.g. abstract) 2- Antioxidant status shall be also performed from the aqueous humor of each patient 3- Data from aqueous humor shall be then compared to serum analysis data 4- Controls: shall specified how the stratification of untreated patients has been performed (intraocular pressure of the controls can be lower than treated patients and this could have biased the interpretation of the data) Please check and provide comparative information 5- Ocuvite® Glaukom : please describe this micronutrients complex in the introduction	1. The reviewer is right. We have changed the manuscript accordingly and mentioned the dose and period of antioxidant supplementation already in the abstract. 2. +3. This is a good point and we hope that we can arrange aqueous humor samples in our next project, which first needs to be approved by the ethics committee. 3. see point 2. 4. The patients who fulfilled the inclusion criteria were randomized to the treated or untreated group. We have clarified this point in the methods section. Furthermore, we have double-checked our raw data and the mean intraocular pressure was similar in both groups. This point is also mentioned in the discussion. 5. The reviewer is right. We added the description of the micronutrient complex in the introduction.



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	6- Table 1: “Subjects” shall be replaced by “patients” – Also, please clarify whether these “subjects” are glaucoma patients treated or untreated with the Ocuville® Glaukom. If they are treated patients, please explain why IP < 20 mmHg was a criterium of inclusion: Indeed, one shall expect inclusion of IP > 20 mmHg... In other words, you should perform experiments with untreated and treated groups of glaucoma patients with IP> 20 mmHg and see how the Ocuville® Glaukom works in this context...In your experimental/clinical conditions, the patients may have a low basal antioxidative status that may hamper significative positive effects of Ocuville® Glaukom... 7- The study is limited by the number of patients...	6. As suggested, we have replaced the word “subjects” by “ patients” in table 1, in table 2 and in the methods and results sections. Patients were randomized to receive tables from either Ocuville Glaukom or placebo. Therefore, both treated and untreated patients were recruited according to the study inclusion (Table 1) and exclusion criteria (Table 2). To clarify this point we have made changes in the micronutritional supplementation part of the method section. This also means that both treated and untreated patients were patients with primary-open angle glaucoma with an intraocular pressure < 20 mmHg controlled only by local antiglaucomatous medication. We wanted to include well-controlled glaucoma patients first to see whether Ocuville Glaukom may have additional positive effects on the antioxidative status of glaucoma patients. We agree to the reviewer that the next step would be to include glaucoma patients who are less well controlled by antiglaucomatous medications alone. 7. The reviewer is right. Therefore this study can only be interpreted as a pilot study as declared in the methods.
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	8- Level of anti-inflammatory markers (enzymes, DNA repair markers) shall have been examined. 9- Examination of the eye shall have been performed at different time points in order to see for improved clinical outcome in treated patients (and not only safety concerns based on "unchanged anomalies" 10- I would like to see HPLC data included in the paper. A simple table is insufficient. 11- In the introduction, you should briefly write about actual treatments including Avastin (Anti-angiogenesis drug) 12- Please include in references the following important publications that summarized well the physiopathology and some genetic aspects of Glaucoma: Menaa F, Braghini CA, Vasconcellos JP, Menaa B, Costa	Further more extensive studies are needed to confirm or disprove our results as mentioned in the discussion. 8. We have thought of this point, however, we wanted to concentrate on the antioxidative status of glaucoma patients in this current project. 9. Some patients were also checked in between (after 6 weeks and 3 months). However, we did not find any improved clinical outcome in treated patients. 10. Table 3 already contains the HPLC results, which was used to determine the concentration of uric acid, ascorbic acid and tocopherol in the serum samples. 11. This is a good point. However, in this study, we examined the antioxidative status and antioxidative effects of micronutrients in glaucoma patients. Avastin as an antiangiogenetic drugs is mainly used for the treatment of surgical filtration blebs in Germany. 12. We have included the mentioned publication in the reference list as reference 1.
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	VP, Figueiredo ES, Melo MB. Keeping an eye on myocilin: a complex molecule associated with primary open-angle glaucoma susceptibility. <i>Molecules</i> . 2011 Jun 27;16(7):5402-21.	
<u>Minor</u> REVISION comments		
<u>Optional/General</u> comments		