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OPEN PEER REVIEW

Non-clinical Safety Evaluation of Camelina Oil: Acute and 12-Week Oral Toxicities

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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Contents

1 **Original submission** Pardis Mohammadi Pour, Mustafa Ghanadian, Associate Editor 2
2 **Revision 1** Mustafa Ghanadian, Associate Editor 4
Authors' reply to reviewers 5
Reviewer and editor comments 8

1 Original submission

3 comments · 16 Oct 2023 – 2 Dec 2023

Pardis Mohammadi Pour Reviewer

MINOR REVISION 16 Oct 2023

Dear Author

I have carefully reviewed your manuscript titled "Non-clinical safety evaluation of Camelina oil: acute and 12-week oral toxicities" and I appreciate the effort you have put into this study. The findings presented in the manuscript are valuable and contribute to our understanding of the safety profile of Camelina oil.

I would like to bring to your attention a few areas that require clarification and improvement in order to enhance the quality and comprehensibility of your manuscript.

1. Determination of fatty acid composition: In the Methods section, you mentioned the use of the Supelcowax 10 column for fatty acid analysis. It would be helpful if you could provide more information about this column, its manufacturer, and whether it has an Agilent J&W Equivalent (DB-WAXetr or HP-INNOWax). Additionally, I kindly request that you provide more detailed information about the experimental conditions, such as the initial oven temperature, the rate of temperature increase, ramping time, and the total run time.

2. "The injection 1:25": Could you please clarify the meaning of this phrase? Is it referring to the split mode used for injection? If so, please provide more information about the specific injection parameters.

3. Table 1: I suggest adding the names of each identified fatty acid, their retention times, and their Kovats indices to enhance the clarity of the table. Furthermore, it would be beneficial to mention the GC-MS library and application that were utilized for fatty acid identification.

4. Identification of fatty acids: It would be helpful if you could explain in the methodology section how the fatty acid results were identified. Which GC-MS library and application were used for this purpose? Did you compare the Kovats indices of each compound?

5. Tables 2-6: I kindly request that you specify that the numbers 250, 500, and 1000 in these tables correspond to the amounts of camelina oil used.

6. Part 3.2: In the second paragraph, I recommend making the comparison of alanine transferase levels between the treated and control groups more explicit and clear.

Overall, I believe that addressing these points will significantly improve the manuscript and make it more accessible to the readers. I appreciate your attention to these suggestions and look forward to seeing the revised version of your manuscript.

Mustafa Ghanadian Reviewer

MINOR REVISION 2 Dec 2023

-Please provide a voucher specimen number for camelina seeds (if available) and identify who identified and confirmed the scientific name of the seeds and plant.
-There are typographical and linguistic errors throughout the manuscript that need correction.
-Please indicate whether the column temperature followed a gradient or was held at a specified temperature (220), because there are several different fatty acids with different b.p. that require a programmed temperature.
-A reference is required for the determination of fatty acids.
-Please add the GC chromatogram of the sample and FAME standards.

-Please describe the method of methylation of fatty acids in this procedure in more detail.
-In the acute oral toxicity study, it is impossible to dilute the oil with pure water for administration by gavage. Please describe the preparation of the oil extract sample in detail.

Associate Editor

MINOR REVISION 2 Dec 2023

Dear Authors,
The manuscript was interesting to me but still needs some corrections.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewer 1:

Dear Author

I have carefully reviewed your manuscript titled "Non-clinical safety evaluation of Camelina oil: acute and 12-week oral toxicities" and I appreciate the effort you have put into this study. The findings presented in the manuscript are valuable and contribute to our understanding of the safety profile of Camelina oil.

I would like to bring to your attention a few areas that require clarification and improvement in order to enhance the quality and comprehensibility of your manuscript.

1. Determination of fatty acid composition: In the Methods section, you mentioned the use of the Supelcowax 10 column for fatty acid analysis. It would be helpful if you could provide more information about the this column Its manufacture and the information like it is Agilent J&W Equivalent (DB-WAXetr or HP-INNOWax). Additionally, I kindly request you to provide more detailed information about the experimental conditions, such as the initial oven temperature, the rate of temperature increase, ramping time, and the total run time.

The section 3 has been revised and some details were added.

2. "The injection 1:25": Could you please clarify the meaning of this phrase? Is it referring to the split mode used for injection? If so, please provide more information about the specific injection parameters.

The section 3 has been revised and some details were added.

3. Table 1: I suggest adding the names of each identified fatty acid, their retention times, and their Kovats indices to enhance the clarity of the table. Furthermore, it would be beneficial to mention the GC-MS library and application that were utilized for fatty acid identification.

We appreciated the reviewer's constructive comments. The name of identified fatty acid and GC-MASS library has been included in the text. It must be noted that in this study, the main objective was to investigate the safety of the Camelina oil. The analysis of the fatty acids was investigated as a small part of the project by Nazgol company with the relevant standards, and the obtained results were sent to this group. Unfortunately, we do not have more information about the fatty acids retention time and Kovats indices. (the report is sent as an attachment).

4. Identification of fatty acids: It would be helpful if you could explain in the methodology section how the fatty acid results were identified. Which GC-MS library and application were used for this purpose? Did you compare the Kovats indices of each compound?

Esterified fatty acids were determined after transesterification according to the AOCS Official Method Ce 1h-05. The identification of the fatty acids was carried out using the National Institute of Standards and Technology (NIST) Mass spectral library. Analysis of fatty acids was done by Nazgol company with test method 2-1-13126.

5. Tables 2-6: I kindly request that you specify that the numbers 250, 500, and 1000 in these tables correspond to the amounts of camelina oil used.

This comment is unclear. The numbers in the tables indicate the amount of camelina oil used.

6. Part 3.2: In the second paragraph, I recommend making the comparison of alanine transferase levels between the treated and control groups more explicit and clear.

Done

Overall, I believe that addressing these points will significantly improve the manuscript and make it more accessible to the readers. I appreciate your attention to these suggestions and look forward to seeing the revised version of your manuscript.

We are very grateful for your time and attention and hope to meet your expectations.

Reviewer 2:

-please prepare a voucher specimen number for camelina seeds (if available) and identify who has identified and confirmed the scientific name of seeds and plant.

It has been added to “Plant collection and extracts preparation “section.

-there are typo linguistic errors through the manuscript which needs correction.

Done

-Please identify which the column temperature was gradient or in a specified temperature (220)? because there are several different fatty acids with different b.p. which require a programmed temperature.

The section 3 has been revised and some details were added.

-for determination of fatty acids reference is required.

This reference was included in the manuscript:

Fallah F, Kahrizi D, Rezaeizad A, Zebarzadi A, Zarei L. (2020). Evaluation of Genetic Variation and Parameters of Fatty Acid Profile in Doubled Haploid Lines of Camelina sativa L. Plant Genetic Researches. 6(2):79-96.

-Please add the gc chromatogram of sample and FAME standards.

We appreciated reviewer's constructive comments. It must be noted that in this study, the main objective was to investigate the safety of the Camelina oil. The analysis of the fatty acids was investigated, as a small part of the project, by Nazgol company with the relevant standards. Unfortunately, we do not have access to GC chromatogram of samples.

-Please add the method of methylation of fatty acids in this procedure with more details.

As mentioned in the previous comment, the analysis of the fatty acids was investigated as a small part of the project by Nazgol company and we don't have access to more details.

-in acute oral toxicity it is impossible to dilute the oil with pure water to be taken by gavage. Please write the preparation of the oil extract sample in details.

We appreciated the reviewer's constructive comments. The different concentrations of oil in the water in form of suspension, was easily administrated to rats using a gavage needle.

2 Revision 1

2 comments · 26 Feb 2024 – 26 Feb 2024

Mustafa Ghanadian Reviewer

ACCEPT 26 Feb 2024

Dear Authors
Thank you for revising the manuscript according to the comments. I think the manuscript could be published at this stage.

Associate Editor

ACCEPT 26 Feb 2024

Dear Authors
The manuscript is OK at this stage. I would like to suggest its publication.