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OPEN PEER REVIEW

A Randomized, Placebo-Controlled Study Investigating the Impact of α-pinene on Symptom Relief, Quality of Life and Inflammatory Markers in Individuals with Ulcerative Colitis

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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** Zahra Shokati Eshkiki, Associate Editor 2
2 **Revision 1** Zahra Shokati Eshkiki 4
Authors' reply to reviewers 5
Reviewer and editor comments 11

1 Original submission

2 comments · 25 Nov 2024 – 3 Dec 2024

Zahra Shokati Eshkiki Reviewer

MAJOR REVISION 25 Nov 2024

Dear Author,

Thank you for submitting your manuscript entitled "The impact of incorporating α-pinene capsules into the medical treatment regimen of patients with ulcerative colitis on symptom relief, quality of life and inflammatory biomarkers" to the Jundishapur Journal of Natural Pharmaceutical Products. Please find the comments below, which I hope will be constructive and helpful.

1. Title:
Considering your results, the selected title is not suitable anymore for this manuscript. Maybe other titles, such as "A randomized placebo-controlled trial on the effects of "α-pinene" on quality of life and inflammatory factors in patients with ulcerative colitis", are more consistent.
2. Abstract:
a) It has to be revised since, in my view, it is not acceptable, comprehensive, or clear.
b) The abstract's language is disorganized and has some spelling mistakes, for example:
- for a duration of two months …
- At the conclusion of …
- Conclusion:Therefore,…
c) It is also necessary to revise the keywords: Ulcerative colitis, α-pinene, Quality of life, randomized clinical trial, inflammatory factors/ESR/CRP…

3. Introduction:
a) Studies should provide general explanations without referencing the authors' names in the introduction section, as opposed to doing so in the discussion section.
b) The introduction section lacks clarity regarding the rationale for studying α-pinene, and it does not provide sufficient background on its significance and relevance for patient use.
c) The last paragraph of the introduction is the most critical component of this section, as it must clearly and succinctly articulate the study's purpose to the reader. Please revise it.
4. Methods:
a) The methodology, especially in clinical trials, should be explained in detail and in separate sections, for example:
- Trial design
- Selection criteria
- Randomization and blinding
- Interventions
- Outcome
- Safety evaluation
- Sample size
- Statistical methods
- Research Ethics
The methodology section requires a more comprehensive presentation, including detailed plans for replicating the work.

b) An important question that arises is the rationale behind the selection of this medication dosage and the duration of two months. Are there any references available that address this issue? Please mention them.

5. Results:

a) In the present study, the number of samples was too small, and the results may not reflect the truth because of this limitation; you cannot draw certain conclusions from the data, and more extensive research is required.

b) I am uncertain about the medication's brand, especially the dose and duration, and I have not seen any references that elucidate this information.

6. Discussion:
The discussion lacks comprehensiveness and sufficient information. The quantity of references is notably insufficient. The discussion section requires additional references for comparative analysis with your work. No conclusion or limitation sections are present.
7. Writing:
The manuscript contains numerous spelling and grammatical errors. Kindly conduct a thorough revision of the document for clarity and adherence to writing standards.

Thank you again for submitting your work.

Associate Editor

MAJOR REVISION 3 Dec 2024

Thank you for submitting your manuscript to JJNPP.
Please revise the manuscript and submit a point-by-point response to the reviewers' comments and concerns.

I would also greatly appreciate the authors' contribution and time spent reviewing manuscripts for this journal. Without the dedication of reviewers like you, it would be impossible to manage an efficient peer review process and maintain the high standards necessary for a successful journal.

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.

Dear editor

Here are our responses to the reviewers

Reviewer 1:
Thank you for submitting your manuscript entitled "The impact of incorporating α-pinene capsules into the medical treatment regimen of patients with ulcerative colitis on symptom relief, quality of life and inflammatory biomarkers" to the Jundishapur Journal of Natural Pharmaceutical Products. Please find the comments below, which I hope will be constructive and helpful.

1. Title:
Considering your results, the selected title is not suitable anymore for this manuscript. Maybe other titles, such as "A randomized placebo-controlled trial on the effects of "α-pinene" on quality of life and inflammatory factors in patients with ulcerative colitis" are more consistent.

Title has been Changed to: A randomized, placebo-controlled study investigating the impact of α-pinene on symptom relief, quality of life and inflammatory markers in individuals with ulcerative colitis

2. Abstract:
a) It has to be revised since, in my view, it is not acceptable, comprehensive, or clear.
b) The abstract's language is disorganized and has some spelling mistakes, for example:
- for a duration of two months …
- At the conclusion of …
- Conclusion:Therefore,…
c) It is also necessary to revise the keywords: Ulcerative colitis, α-pinene, Quality of life, randomized clinical trial, inflammatory factors/ESR/CRP…

Grammatical errors have been corrected (in red color). Also, Key words have been changed to: Ulcerative colitis, α-pinene, Quality of life, randomized clinical trial, Inflammatory markers, ESR, CRP

3. Introduction:
a) Studies should provide general explanations without referencing the authors' names in the introduction section, as opposed to doing so in the discussion section.
b) The introduction section lacks clarity regarding the rationale for studying α-pinene, and it does not provide sufficient background on its significance

and relevance for patient use.
c) The last paragraph of the introduction is the most critical component of this section, as it must clearly and succinctly articulate the study's purpose to the reader. Please, revise it.

a) the name of authors has been deleted from introduction and discussion. We have written "in a clinical study".... Instead of " the name of author at the begging part"

b, C) these sentences have been added (in red color at the end of introduction):The comprehensive impact of α-pinene, the principal component of mastic gum, has not been previously assessed. Additionally, prior research has predominantly focused on some inflammatory markers in patients with UC.

4. Methods:
a) The methodology, especially in clinical trials, should be explained in detail and separate sections, for example:Trial design,Selection criteria, Randomization and blinding,Interventions, Outcome, Safety Evaluation, Sample size, Statistical methods,Research Ethics
The methodology section requires a more comprehensive presentation, including detailed plans for replicating the work.

Separate sections have been designed (in red color).

b) An important question that arises is the rationale behind the selection of this medication dosage and the duration of two months. Are there any references available that address this issue? Please mention it.

There is currently no data available on the effective dose of α-pinene for UC. However, a recent trial has demonstrated a positive effect of α-pinene at a dose of 0.2 g/day in functional dyspepsia, with no serious adverse reactions reported. Therefore, we have opted to use the same dosage. Regarding the duration of the trial, the standard period for evaluating changes in drug regimens for UC is typically 2 months, and we have adopted this timeframe for follow-up. We have added a sentence regarding this in the methods (in red color).

5. Results:

a) In the present study, the number of samples was too small, and the results may not reflect the truth, because of this limitation; you cannot draw certain conclusions from the data, and more extensive research is required.

We have calculated sample size on the basis of similar trials but we have added to the limitation and suggestion for future studies at the end of the discussion.

b) I am uncertain about the medication's brand, especially the dose and duration, and I have not seen any references that elucidate this information?!

There is currently no data available on the effective dose of α-pinene for UC. However, a recent trial has demonstrated a positive effect of α-pinene at a dose of 0.2 g/day in functional dyspepsia, with no serious adverse reactions reported. Therefore, we have opted to use the same dosage (in red color).

6. Discussion:
The discussion lacks comprehensiveness and sufficient information. The quantity of references is notably insufficient. The discussion section requires additional references for comparative analysis with your work. No conclusion or limitation sections are present.

We conducted a comprehensive search in PubMed and SCOPUS, revealing a limited number of published human trials concerning the use of mastic gum and α-pinene in the treatment of UC. The majority of the published manuscripts have been cited in our study.

Limitations have been added at the end of discussion: In future studies, we propose the assessment of fecal calprotectin as a significant biomarker for UC to investigate potential differences between groups. Given that the inhibition of IL-1β is likely the mechanism by which α-pinene alleviates UC symptoms, it is highly recommended that future clinical trials evaluate this biomarker. Additionally, given the safety profile of α-pinene, we recommend evaluating its effects at higher doses. Our study was constrained to a dosage of 0.2 mg/day of α-pinene, and it is plausible that this dosage is insufficient to elicit a positive response on inflammatory biomarkers. Considering the favorable safety profile of α-pinene, we advocate for the assessment of its effects at higher dosages.

Conclusion has been added: The findings of our study indicate that adjuvant α-pinene therapy at a dosage of 0.2 g/day over a two-month period is relatively safe. Furthermore, it may contribute to the amelioration of clinical signs and symptoms, as well as the enhancement of QoL in patients with UC.

7. Writing:

The manuscript contains numerous spelling and grammatical errors. Kindly conduct a thorough revision of the document for clarity and adherence to writing standards.

The manuscript has been revised.

Reviewer 2:
This manuscript deals with " The impact of incorporating α-pinene capsules into the medical treatment regimen of patients with ulcerative colitis on symptom relief, quality of life and inflammatory biomarkers" I suggest a minor correction and require a detailed clarification. This is an interesting work and well presented. I severely suggest accepting the recent manuscript in the Jundishapur Journal of Natural Pharmaceutical Products. If it is accepted, it will have an excellent role in increasing the citation and the Impact Factor of Jundishapur Journal of Natural Pharmaceutical Products in the future. A correction should be addressed by the authors as follows:

1. Correct grammatical error and typo error.

corrected
2. Suitable reference should be cited in therapeutic activity.

We conducted a comprehensive search in PubMed and SCOPUS, revealing a limited number of published human trials concerning the use of mastic gum and α-pinene in the treatment of UC. The majority of the published manuscripts have been cited in our study.

3. Improve the quality of figures.

Improved
4. Source of materials must be reported.

Added (in red color in the method)
5. Mention the limitation of the study before the References.

Limitations havse been added at the end of discussion: In future studies, we propose the assessment of fecal calprotectin as a significant biomarker for UC to investigate potential differences between groups. Given that the inhibition of IL-1β is likely the mechanism by which α-pinene alleviates UC symptoms, it is highly recommended that future clinical trials evaluate this biomarker. Additionally, given the safety profile of α-pinene, we recommend evaluating its effects at higher doses. Our study was constrained to a dosage of 0.2 mg/day of α-pinene, and it is plausible that this dosage is insufficient to elicit a positive response on inflammatory biomarkers.

Considering the favorable safety profile of α-pinene, we advocate for the assessment of its effects at higher dosages.

6. Please check the references according to the journal format.

Modified

7. Conclusion is weak, please progress it.

Conclusion has been added: The findings of our study indicate that adjuvant α-pinene therapy at a dosage of 0.2 g/day over a two-month period is relatively safe. Furthermore, it may contribute to the amelioration of clinical signs and symptoms, as well as the enhancement of QoL in patients with UC.

8. Other therapeutic effects may be investigated.

Added in red color at the beginning of discussion.

9. Increase the resolution of Figures.

Improved

10. Bold the aim of the study in the Introduction.

Added (in red color at the end of introduction): The objective of the current clinical trial is to evaluate the efficacy and safety of α-pinene capsule administration (derived from Pistacia kurdica) as an adjuvant therapy for alleviating symptoms of UC and improving patients' QoL (primary outcomes). The secondary outcome involves assessing the impact of α-pinene on optimizing laboratory markers in UC patients.

11. Please mention the details of statistical analysis.

Added in statistical analysis: The means of age, BMI, duration of UC, SCCAIQ score, items of CUCQ-8, ESR, and CRP were compared within groups using the t-test for normally distributed data or the Mann-Whitney test for non-normally distributed data. For the comparison of categorical variables, including sex distribution and differences in medication use between the two groups, the chi-square test was employed (in red color).

13. Use the available drug as the positive control and compare your formulation with it.

All patients received standard medications for ulcerative colitis (as detailed in Table 1). We then compared the effects of adding α-pinene or a placebo to this medical regimen. "It is important to note that there was no difference in the pharmacotherapy regimen of the UC patients between the α-pinene and placebo groups during the study period (p=0.02)." in discussion in red color.

14. The results are well prsented, but no discussion and comparison with similar results has been done.

Discussion has been revised and some sentences have been added (in red color)

Cheers

Correspondence

2 Revision 1

1 comment · 18 Dec 2024

Zahra Shokati Eshkiki Reviewer

ACCEPT 18 Dec 2024

We appreciate your submission of the article titled "A randomized, placebo-controlled study investigating the impact of α-pinene on symptom relief, quality of life and inflammatory markers in individuals with ulcerative colitis" to the Jundishapur Journal of Natural Pharmaceutical Products. The errors have been corrected, and the article has been accepted.