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OPEN PEER REVIEW

Phytochemical Composition of *Rosa foetida* Essential Oil and Evaluation of Antioxidant and Anti-oral Squamous Cancer Activities

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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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1 Original submission

2 comments · 16 Sep 2024 – 23 Sep 2024

Referee 1 Reviewer

MINOR REVISION 16 Sep 2024

The article titled "Phytochemical composition of Rosa foetida essential oil and evaluation of antioxidant and anti-oral squamous cancer activities" is well-organized. To further enhance the quality and relevance of the work, I have a few suggestions that could strengthen the impact of the manuscript.

1. Why were the specific oral squamous cell carcinoma lines (HSC-2, HSC-3, HSC-4, Ca9-22) chosen for this study? What is their relevance in the context of oral cancer research?
2. Were appropriate control groups used in the MTT assay (e.g., untreated controls, solvent controls)? How were these controls selected?
3. Did the authors explore or discuss the potential mechanisms by which R. foetida essential oil exerts its cytotoxic effects on the cancer cell lines?
4. Please consider including more recent articles from the last five years to enhance the relevance of the references.

Associate Editor

MAJOR REVISION 23 Sep 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 your contribution and the time you spend 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.

Best Regards

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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.

16 December 2024

Dear Professor Nguyen Huu Duc

Editor-in-Chief of Jundishapur Journal of natural Pharmaceutical Products

Manuscript ID: 154003

Manuscript title: Phytochemical composition of *Rosa foetida* essential oil and evaluation of antioxidant and anti-oral squamous cancer activities

Thank you for your letter dated 23 September 2024. we were pleased to know that our manuscript was rated as potentially acceptable for publication in Jundishapur Journal of natural Pharmaceutical Products, subject to adequate revision and response to the comments raised by the reviewers.

Based on the instructions provided in your letter, we uploaded the file of the revised manuscript to the journal's website.

As you noticed, we have revised the manuscript by modifying the Abstract, Introduction, Methods, Results and discussion based on the comments made by reviewers, Accordingly, we have uploaded a copy of the original manuscript marked in yellow color with all the changes made during the revision process.

Appended to this letter is our point-by-point response to the comments raised by the reviewers. As you notice, we agreed with all the reviewers' comments. We would like to take this opportunity to express our sincere thanks to the reviewers who identified areas of our manuscript that needed corrections to modification. We would like also to thank you for allowing us to resubmit a revised copy of the manuscript.

We hope that the revised manuscript is accepted for publication in Jundishapur Journal of natural Pharmaceutical Products. Sincerely,

Sincerely,

On behalf of the authors

Corresponding author

Reviewers' Comments:

Reviewer 1:

The manuscript entitled “Phytochemical composition of Rosa foetida essential oil and evaluation of antioxidant and anti-oral squamous cancer activities” is an interesting manuscript. However, suffers from some major defects that needs to be addressed listed below:

1. What specific criteria did you use to select the cell lines (HSC-2, HSC-3, HSC-4, and Ca9-22) for evaluating the anti-cancer activity of Rosa foetida essential oil?

Answer: The comment was replied in “2. Objectives” as the best. Please see:

“Due to the Rosa foetida is used for the treatment of oral diseases in the traditional medicine [10-12], we focus on the extraction of the essential oil of Rosa foetida and the identification of chemical composition as well as the anticancer activity of the plant essential oil against oral malignancy cell lines using MTT assay for the first time, also the extract of Rosa foetida and the evaluation of antioxidant activity of the plant extract in the present study. The common HSC-2, HSC-3, HSC-4, and Ca9-22 oral malignancy cell lines were used for determining the anticancer effects of the Rosa foetida essential oil in vitro condition.”

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2. Could you provide more details on the potential biological activities of the identified major compounds (heneicosane, tricosane, nonadecane) in the essential oil?

Answer: Thank you for your valuable comment, we provide some information to show the biological activities of these components in section 4.2.

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3. How do your findings regarding the chemical composition of R. foetida essential oil compare with previous studies on other rose species? What implications does this have for the understanding of its medicinal properties?

Answer: Thank you for your valuable comment. Rose species are popular due to their antioxidant activities, which cause the biological effects mentioned in section 5.3.

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4. Did you investigate the specific mechanisms through which Rosa foetida essential oil exerts its anti-cancer and antioxidant effects?

Answer: Thank you for your valuable comment. Responses to the respectable reviewer comment: The comment was applied in “5.2. Anticancer activities” as the best. Please see:

"Many radical-producing agents such as plants are used in the treatment of cancer tumors. In this case, the production of radicals and toxic or mutagenic side effects that damage healthy tissues can be well controlled [28]. Plant extracts such as Rosa foetida as pharmaceutical carriers can solve some of the current drug delivery limitations in cancer treatment. It seems that the anti-human oral squamous cell carcinoma effect of recent essential oils is because of their antioxidant effects[29]. Recent studies have confirmed that some components of Rosa foetida play a great role in anticancer, antioxidant, and anti-inflammatory activities. These components mostly contain aromatic ones such as eugenol, thymol, carvacrol limonene, etc. which means plants that include this kind of component can show anticancer, antioxidant, and anti-inflammatory activities. Based on the result of the MTT assay and identified components the anticancer activity of Rosa foetida should be related to the presence of these components in the essential oil[30]."

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5. What control measures were implemented in your experiments to ensure the reliability of the MTT and DPPH assays?

Answer: Responses to the respectable reviewer comment: Methanol was used as a negative control in DPPH assay, while DMSO was used as a negative control in MTT assay.

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6. Could you elaborate on the statistical methods used to analyze the data, and how you determined the significance of your results?

Answer: The comment was applied in "2.9. Statistical analysis" as the best.

"The biological effects of the essential oil were assessed, and notable differences were analyzed utilizing SPSS-22 software along with one-way ANOVA. The calculations were conducted with a confidence level set at 0.01."

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7. Can you discuss the potential health benefits associated with the total phenolic and flavonoid content you measured, and how they relate to the observed biological activities?

Answer: Thank you for your valuable comment. We discuss the connection between phenolic and flavonoid components and antioxidant activities. In addition, how they can affect body reactions in section 5.3.

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8. What considerations did you take into account when choosing the hydro-distillation method for extracting the essential oil, and how might this influence the composition of the oil?

Answer: Thank you for your valuable comment. We discuss the influences and our considerations when choosing the hydro-distillation method in section 5.1.

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9. From linguistic and grammatical perspective:

• A) Example: The phrase "the essential oil of R. foetida flowers was isolated to identify the chemical composition and evaluation of anti oral cancer and antioxidant activity of the plant extract" could be clearer.

Answer: Thank you for your valuable comment. It corrected in Abstract section.

• B) Issue: The article switches between "R. foetida" and "Rosa foetida" without a clear pattern.

Answer: Thank you for your valuable comment. A single format selected.

• C) Example: In the phrase "anti oral cancer and antioxidant activity," "anti oral cancer" should be hyphenated as "anti-oral cancer."

Answer: Thank you for your valuable comment. These words changed to the correct format.

• D) Issue: The article sometimes shifts tenses, which can confuse readers.

• E) Example: "The compounds are mainly related to the pleasant aroma of the rose species."

Answer: Thank you for your valuable comment. It considered in the text.

• F) Issue: Some phrases are redundant or overly complex.

• Example: "The essential oil was dominated by heneicosane (27.72%), tricosane (24.30%), and nonadecane (14.75%)."

Answer: Thank you for your valuable comment. These complex phrases modified in the text.

• G) Issue: While technical terms are necessary, excessive jargon can alienate readers.

Answer: Thank you for your valuable comment. The explanation of technical methods added in sections 3.2, 3.3 & 5.1.

• H) Issue: Some sections lack smooth transitions, making it hard to follow the narrative.

Answer: Thank you for your valuable comment. **It considered in the text.**

Reviewer 2:

1. Why were the specific oral squamous cell carcinoma lines (HSC-2, HSC-3, HSC-4, Ca9-22) chosen for this study? What is their relevance in the context of oral cancer research?

Answer: Thank you for your comment. The comment was replied in "2. Objectives". Please see: "Due to the Rosa foetida is used for the treatment of oral diseases in the traditional medicine [10-12], we focus on the extraction of the essential oil of Rosa foetida and the identification of chemical composition as well as the anticancer activity of the plant essential oil against oral malignancy cell lines using MTT assay for the first time, also the extract of Rosa foetida and the evaluation of antioxidant activity of the plant extract in the present study. The common HSC-2, HSC-3, HSC-4, and Ca9-22 oral malignancy cell lines were used for determining the anticancer effects of the Rosa foetida essential oil in vitro condition."

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2. Were appropriate control groups used in the MTT assay (e.g., untreated controls, solvent controls)? How were these controls selected?

Answer: while DMSO was used as a negative control in MTT assay.

---

3. Did the authors explore or discuss the potential mechanisms by which R. foetida essential oil exerts its cytotoxic effects on the cancer cell lines?

Answer: The comment was applied in "5.2. Anticancer activities" as the best. Please see:

"Many radical-producing agents such as plants are used in the treatment of cancer tumors. In this case, the production of radicals and toxic or mutagenic side effects that damage healthy tissues can be well controlled [28]. Plant extracts such as Rosa foetida as pharmaceutical carriers can solve some of the current drug delivery limitations in cancer treatment. It seems that the anti-human oral squamous cell carcinoma effect of recent essential oils is because of their antioxidant effects[29]. Recent studies have confirmed that some components of Rosa foetida play a great role in anticancer, antioxidant, and anti-inflammatory activities. These components mostly contain aromatic ones such as eugenol, thymol, carvacrol limonene, etc. which means plants that include this kind of component can show anticancer, antioxidant, and anti-inflammatory activities. Based on the result of the MTT assay and identified components the anticancer activity of Rosa foetida should be related

to the presence the anticancer activity of Rosa foetida should be related to the presence of these components in the essential oil[30].”

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4. Please consider including more recent articles from the last five years to enhance the relevance of the references.

Answer: Thank you for your valuable comment. **These following articles added.**

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[17] V. Vanitha, S. Vijayakumar, Heneicosane—A novel microbicidal bioactive alkane identified from Plumbago zeylanica L, Industrial Crops and Products, 154 (2020) 112748.

[18] P.N. Okechukwu, Evaluation of Anti-Inflammatory, Analgesic, Antipyretic Effect of Eicosane, Pentadecane, Octacosane, and Heneicosane, Asian Journal of Pharmaceutical and Clinical Research, 13 (2020) 29-35.

[19] C. Tao, J. Wu, Antimicrobial activities of bamboo (Phyllostachys heterocycla cv. Pubescens) leaf essential oil and its major components, European Food Research and Technology, 244 (2018) 881-891.

[26] P.S. Pavithra, A. Mehta, Induction of apoptosis by essential oil from P. missionis in skin epidermoid cancer cells, Phytomedicine, 50 (2018) 184-195.

[40] L.A. Sampaio, L.T.S. Pina, Antitumor Effects of Carvacrol and Thymol: A Systematic Review, Frontiers in Pharmacology, 12 (2021).

2 Revision 1

1 comment · 24 Dec 2024

Referee 1 Reviewer

ACCEPT 24 Dec 2024

The manuscript has been satisfactorily corrected.

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Revision 2

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.

29 December 2024

Dear Professor Masood Fereidoonnezhad

Editor-in-Chief of Jundishapur Journal of natural Pharmaceutical Products

Manuscript ID: 154003

Manuscript title: Phytochemical composition of *Rosa foetida* essential oil and evaluation of antioxidant and anti-oral squamous cancer activities

Thank you for your letter dated 29 December 2024. we were pleased to know that our manuscript was rated as potentially acceptable for publication in Jundishapur Journal of natural Pharmaceutical Products, subject to adequate revision and response to the comments raised by the reviewers.

Based on the instructions provided in your letter, we uploaded the file of the revised manuscript to the journal's website.

As you noticed, we have revised the manuscript by modifying the Abstract and discussion based on the comments made by reviewers, Accordingly, we have uploaded a copy of the original manuscript marked in yellow color with all the changes made during the revision process.

Appended to this letter is our point-by-point response to the comments raised by the reviewers. As you notice, we agreed with all the reviewers' comments. We would like to take this opportunity to express our sincere thanks to the reviewers who identified areas of our manuscript that needed corrections to modification. We would like also to thank you for allowing us to resubmit a revised copy of the manuscript.

We hope that the revised manuscript is accepted for publication in Jundishapur Journal of natural Pharmaceutical Products. Sincerely,

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Reviewers' Comments:

Reviewer 1:
Comment: The manuscript has been satisfactorily corrected.

Answer: Thank for your comment

Reviewer 2:
comment: There still needs some minor revisions: In your manuscript, you state the value as "164 ± 0.67." However, this presentation may not convey statistical significance effectively. Could you clarify whether this value should be reported as "164.00 ± 0.67" to better reflect the precision of your measurements?
Or, you report values such as "6.54 ± 0.2." Could you provide clarification on the precision of these measurements? Specifically, would it be more appropriate to express these values with additional decimal places (e.g., "6.54 ± 0.20") to accurately reflect the level of precision in your data?

Answer: Thank for your valuable comment, the correction has been done according to the comment. The all values have been corrected by 2 decimal (0.00)

Reviewer 3:
Comment: Acceptance

Answer: Thank for your comment

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3 Revision 2

0 comments

No public comments in this round.