

Author's Response

Responses to reviewers' comments for “**The phytochemical profile and unveiling of the promising potential of *Purslane* petroleum ether extract in combating lung cancer induced by 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in rats.**” (Manuscript ID: ijms-3271464).

Dear Editor,

We thank the reviewers for their insightful comments, which enabled us to improve the manuscript. We hope that you will accept it after revision. According to the reviewers' suggestions, the manuscript has been revised carefully. The detailed corrections raised by the reviewers have been addressed point by point and highlighted in yellow in the revised manuscript.

Reviewer 2

In the manuscript (ID: ijms-3271464) studied, the phytochemical profile of *Purslane* petroleum ether extract and its anti-4- (methylnitrosamine)-1-(3-pyridyl) -1-but-4 none (NNK) induced lung cancer in rats were studied. Generally, the content of this manuscript meets the requirements of International Journal of Molecular Sciences. Therefore, I think that the manuscript can be accepted published in International Journal of Molecular Sciences after a major revision.

Response: A lot of thanks to the reviewer for this comment.

Commented 1: (1) Title

Line 2-5: The title is too long and the meaning is not clear enough. Should be “The phytochemical profile of *Purslane* petroleum ether extract and its anti- 4-(Methylnitrosamino)-1-(3-pyridyl)-1-buta-4 none (NNK) indiced lung cancer in rats” rather “The phytochemical profile and unveiling of the promising potential of *Purslane* petroleum ether extract in combating lung cancer induced by 4-(Methylnitrosamino)-1-(3-pyridyl)-1-buta-4 none (NNK) in rats.”.

Response 1: We thank the reviewer for his comments, which enabled us to improve our work. We changed the title to “The phytochemical profile of *Purslane* leaves petroleum ether extract and its anticancer effect on 4-(Methylnitrosamino)-1-(3-pyridyl)-1-buta-4 none (NNK) induced lung cancer in rats.”

Commented 2: (2) Abstract

- Line 25: Should be “petroleum ether extract of purslane leaf” rather “purslane leaf petroleum ether extract”.

Response: Comment is made, line 24.

- Line 26: Should be “4-(Methylnitrosamino)-1-(3-pyridyl)-1-buta-4 none (NNK)” rather “NNK”.

Response: Comment is made.

- Line 26: Should be “in vitro” rather “in-vitro”. In addition, “in vitro” should be in italics. In addition, there are similar errors in other parts of the manuscript, and authors are advised to check the whole manuscript carefully and correct these minor errors.

Response: Comment is made throughout the manuscript.

- Line 29 and 34: Please provide the full name of ICAM and FOXO1. When an abbreviation appears in the manuscript, write its full name first, and the abbreviation is written after the full name in parentheses. Subsequently, use the abbreviation consistently and do not write out the full term again.

Response: Comment is made, and all abbreviations in the abstract are written in full names.

- Line 39: Should be “LC-MS, including” rather “LC-Mass, such as”.

Response: Comment is made.

Commented 3: (3) Keywords

Suggest the author to add this keywords of “Purslane leaf”, “Phytochemical profile” and “lung cancer”. Besides, these keywords inducing Intercellular Adhesion Molecule-1(ICAM-1) and proliferation don't seem necessary

Response 3: Comment is made.

Commented 4: (4) Introduction

- Line 44: Should be “1. Introduction” rather “Introduction:”. Please read the submission requirements of International Journal of Molecular Sciences and revise the title carefully.

Response: Comment is made through the manuscript.

- In this manuscript, the review of phytochemicals to treat lung cancer lacks depth. Presently, there's a lot of research going on using phytochemicals to treat lung cancer, such as phytochemical composition and anticancer effect of Akebia trifoliata seed in non-small cell lung cancer A549 cells, Phytochemical composition and anticancer effect of Akebia trifoliata seed in non-small cell lung cancer A549 cells, etc. It is suggested that the authors systematically review the activity and structure of these ACE inhibitory peptides, so as to further explain the innovation, importance and significance of this study.

Response

- Line 80-81: Should be “fibrosis [18].” rather “fibrosis. [18]”.

Response: Comment is made.

- Line 84: Should be “cancer [26].” rather “cancer. [26]”. In addition, there are similar errors in other parts of the manuscript, and authors are advised to check the whole manuscript carefully and correct these minor errors.

Response: Comment is made.

- Line 97: Should be “(i) unveil” rather “(i) Unveil”.

Response: Comment is made.

Commented 5: (5) Results and discussion

- Line 102-115: When we planned this study ... we studied its effect on the safety profile in diseased and healthy animals. LC-QTOF-HR-MS/MS studied the metabolites of the Purslane Pet. ether extract. In the results and discussion section, the author does not need to repeat the research purpose and research method. The authors are advised to delete this section.

Response: The paragraph is removed from the manuscript.

- Line 119, 121 and 122: Why the deepening of "A549"?

Response: The deepening is removed.

- Figure 2: Data analysis, especially significance analysis, should be applied to all experimental results of the manuscript.

Response: A significance analysis was added in Figure 2 of the manuscript.

- Line 116 and 132: “1.1. The Study on the A549 lung cancer cell line (in vitro investigation):” and “1.1. The study on the experimental animals (in vivo investigation):”. There is a problem with the serial number of the title. In addition, there is no serial number in the previous title, and here the serial number appears. The impression from this manuscript is that it was edited in hurry, resulting in many formatting errors and confusion.

Response: The serial numbers of titles are corrected throughout the manuscript.

- Figure 3B: It is suggested that all figures in this manuscript should have scales on their vertical axes, just like Figure 4B. In addition, please check the ordinate values of this figure carefully.

Response: The comment is made.

- Figure 11 and Table 1: Authors are advised to present key data in the main text, while other data can be used as supplementary material.

Response: Dear reviewer

Please keep this section because we work in a team work and each of us has his own specialty. In this specialty, three authors work in the field of plant phytochemistry, and this research is presented to promote each in his field; they played this role in the manuscript because their specialty is to interpret, define, and identify the polyphenolic components using HPLC-QTOF-MS/MS. This section includes evidence and explanations for the presence of these anti-lung cancer compounds. If this section is deleted, this means that this research team did not cooperate in this work and thus cancels the role that they originally performed. Please understand the problem that will return to

the team of this specialty that performed the work seriously for this section and please, accept the existence of this section in the manuscript as we are grateful to you.

Commented 6: (6) Materials and methods

- 1.1. Chemicals: Each material and reagents used should include Brand, catalog number, company, and the city and the country of company located.

Response: Brand, company, and the city and the country of company located of all kits and chemical are places. Lines 867-877 and 972-979.

- Line 867-877: “1.1. Chemicals” and “1.1. Authentication of the plant and extraction”. The serial number of the title in this manuscript is all wrong. It is recommended that the author carefully modify it, otherwise the manuscript cannot be accepted for publication.

Response: The serial numbers of titles are corrected throughout the manuscript.

- Line 888: Should be “1.1. The study on A549 lung cancer cell line (in vitro investigation)” rather “1.1. The Study on The A549 lung cancer cell line (in vitro investigation):”. It is recommended that authors carefully read the submission requirements of International Journal of Molecular Sciences, confirm whether the first letter of each word in the title needs to be capitalized, and unify the writing of the words in the title.

Response: Comment is made throughout the manuscript.

- Line 923: Should be “(20–25 °C” rather “(20–25 Co”.

Response: Comment is made.

Thank you for your attention and help!

Yours Sincerely,

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