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OPEN PEER REVIEW

Froriepia subpinnata Leaf Extract-Induced Apoptosis in the MCF-7 Breast Cancer Cell Line by Increasing Intracellular Oxidative Stress

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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

1 comment · 6 May 2023

Associate Editor

MAJOR REVISION 6 May 2023

Dear authors
Please check the referees' comments. In summary, please include data for a normal cell such as MCF-10 for the MTT test, and it is also advisable to perform HPLC chromatography fingerprinting at least for the control of one of the chemical constituents of the extracts.

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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.

Editor and Reviewer comments:

Author response:

Dear Reviewers:

Thank you for taking the time to provide your expert and experienced feedback on our research. We are grateful for your insights and hope that the explanations we provide in this response will clarify any questions or concerns you may have had. Please accept our apologies for the delay. Unfortunately, we ran into some problems to conduct laboratory tests and this process took time.

Reviewer #1:

The manuscript: Froriepia subpinnata leaves extract induced apoptosis in the MCF-7 breast 2 cancer cell line through increasing in intracellular oxidative stress

describe the extraction of the plant material with methanol followed by determination of its cytotxicity against the breast cancer cell line in vitro test. Then the authors determine the mechanisms of apoptosis for the extract, etc. Although determination of anticancer activity is very important, But It is suggested that the author did it for the pure compounds isolated from the plant material. Or if they want to do it, it is advisable to run a chromatography finger printing at least for control the chemical constituents of the extracts for further research. At the preset without a TLC or HPLC chromatogram, I do not suggest the paper for publication.

on the other hand usually it is better to use different solvents to extract various metabolites then screen for the test and select the best for further analyses.

Author response:

In response to the request of the expert reviewer, since the main compounds of the Apiaceae family are volatile compounds, we used GC-MS analysis to indicate *Froriepia subpinnata*'s main compounds. Contentedly, the results of the GC-MS analysis showed a great alignment with the previous results and could better support them.

The GC-MS analysis method and results are added in lines 77 and 146. Also, the anti-cancer properties of the most abundant plant compounds have been investigated in the discussion section in line 233.

Regarding the HPLC chromatogram, we should mention that this test is performed on non-volatile compounds. We faced a lack of facilities because the relevant laboratories wanted the extract to be fractionated in order to use HPLC different columns to accurately detect the compounds of this plant, which was a time-consuming and costly process. Since most compounds of the Apiaceae family and especially *Froriepia subpinnata* are volatile, we decided to use the GC-MS analysis to determine its main compounds. We hope this test will be convincing for the respected reviewer. We tried our best to convince the reviewer with the facilities and time we had.

Thank you again for your valuable comments, and we look forward to continued engagement in this important area of research.

All the changes regarding reviewer-1's comments were highlighted in green in the manuscript.

Reviewer #2:

This work report apoptotic effects of F. subpinnata extract. Before it could be considered for publication, some comments should be addressed:

Author response:

Thank you for taking the time to read this article. We acknowledge that our study may have some weaknesses, including the absence of healthy cell control. As it was said, we added the MCF-10 cell line to the article to create more clarity. This can help improve interpretation and make it more accurate. The experiment was designed to ensure that the results would support each other and the discussion. The MCF-10A culturing is added to the material and method in line 90 and the result is reported in line 159. Also, it is added in Figure 1 part B.

We tried to conduct the test adequately and decently. I hope the honorable reviewer is satisfied with the results.

All the changes regarding reviewer-1's comments were highlighted in yellow in the manuscript.

1-Absrtact :

Abbreviations (NAC) should not be used in the abstract.

The unit of IC50 must be included

Author response:

We have corrected this in the abstract and highlighted it. Also, the unit of IC50 is included.

2-Introduction:

Please refer to the study which evaluated antibacterial effects of this plant extract. Why authors chose breast cancer cells to evaluate the effect of this plant extract? Please explain more in the introduction

Author response:

As requested by the expert reviewer, this information has been included in the introduction in line 63.

The topic of chosen breast cancer cells to evaluate the effect of this plant extract requested by the respected reviewer was included in the Interdiction (lines 32-36).

3-Method:

How many cells were treated in Flow cytometry analysis

Author response:

We have used sixty thousand cells for each repetition and this issue is added to the manuscript according to the reviewer’s comment (line 132).

4-Results

Please mention the number of repeat (n) for each experiment in the figure legends

Author response:

This issue has been corrected at the request of the respected reviewer

5-Discussion

This section can be expanded to include more the similar results from Apiaceae family

Author response:

The topic requested by the respected reviewer was included in the discussion (lines 228-230)

Associate Editor's Comments:

Associate Editor 1:

Dear authors

Please check the referees comments. In summary please include the data of a normal cell like MCF-10 for MTT test, and it is also advisable to run an HPLC chromatography finger printing at least for the control of one of the chemical constituents of the extracts.

Author response:

I would like to thank you for taking the time to improve our study. We tried our best to address all respected referees' concerns. Performing the requested laboratory tests took time and caused the delay. Please accept our apologies. I appreciate your time and consideration. We hope that the desired changes have been made for you.

Yours sincerely

2 Revision 1

0 comments

No public comments in this round.

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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.

Editor and Reviewer comments:

Reviewer #1:

minor revision

abstract

The unit of IC50 must be included. 400???

Author response:

We appreciate your time and effort in reviewing our study. The requested items were applied in the abstract and highlighted in yellow. Also worth mentioning, we added a new reference on line 48 to the manuscript.

Associate Editor's Comments:

Associate Editor 1:

Dear Authors

The manuscript could be accepted but after minor revision.

Author response:

Your review of our study is greatly appreciated. We have made some changes to the author information section. In the case of the third person, another affiliation was added.

Yours sincerely

3 Revision 2

2 comments · 14 Aug 2023 – 16 Aug 2023

Referee 1 Reviewer

ACCEPT 14 Aug 2023

Dear Authors
Thank you for implementing the reference and IC50 units. My suggestion is acceptance of the article at this stage.

Associate Editor

ACCEPT 16 Aug 2023

Dear Authors
Thank you for making the minor revision. The article could now be accepted as it is.