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OPEN PEER REVIEW

Improvement of Cyclosporin A Production in the fungus *Tolypocladium inflatum* PTCC 5253 by Random Mutagenesis

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1 Original submission

3 comments · 28 Sep 2024 – 30 Dec 2024

Referee 1 Reviewer

MAJOR REVISION 28 Sep 2024

Dear Editor
High-yield production of CysA is of great importance. However, special derivatives of CysA are also developed.
-The source of the fungus (Tolypocladium inflatum PTCC 5253) is not clear. Is it a gift or supplied from a known source? There is the possibility that the sequence of CysA is modified.
- Authors are required to show the MW of CysA produced by the WT and mutant fungi.
-Authors are required to report whether the peptide is secreted by the irradiated fungus or is produced by its next generation. In the latter case, the work is significantly important.
-The details of the instruments employed (LC/MS), as well as the data obtained, should be included in the MM and Results sections.
-Some figure labels are typed in Persian.
-Authors are required to provide suitable REFERENCE(S) for UV irradiations.
-Statistical issues like SEM/SD or triplicates/duplicates should be checked by an expert.
-Authors are required to provide some suitable references/evidence to correlate “increased viscosity” of the medium with an increased concentration of CysA.

Ref.
Bio-synthesis, purification and structural analysis of Cyclosporine-A produced by Tolypocladium inflatum with valorization of agro-industrial wastes

Associate Editor

MAJOR REVISION 30 Dec 2024

Dear Authors,

We appreciate your submission of the article entitled “Improvement of Cyclosporin A production in the fungus Tolypocladium inflatum PTCC 5253 by random mutagenesis” to the Journal of Reports in Pharmaceutical Sciences. After careful review, we have decided that your manuscript requires major revisions before it can be considered for publication.

Please submit your revised manuscript along with a point-by-point response to the reviewers’ comments at your earliest convenience. If you have any questions or need further clarification, do not hesitate to contact us.

Thank you for your contributions to the field, and we look forward to your revised submission.

Best regards,
E.I.C
Journal of Reports in Pharmaceutical Sciences

Editor-in-Chief

MAJOR REVISION 30 Dec 2024

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Journal of Reports in Pharmaceutical Sciences

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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.

January 2025 4

Dear Professor Dr. Gholamreza Bahrami

Editor-in-Chief of Journal of Reports in Pharmaceutical Sciences

Thank you and the reviewers sincerely for your considerations on our manuscript. The responses for reviewers' comments are listed in the following. The changed parts of manuscript are highlighted in the red color in the attached revised manuscript.

Thank you again,

Sincerely yours,

A. D., Pharm.D., PhD

Reviewer 1:

Dear Editor

High yield Production of CysA is a great of importance. However, the special derivatives of CysA is also developed.

1. -The source of the (*Tolypocladium inflatum* PTCC 5253) Fungus is not clear. Is it a gift or supplied from a known source? There is the possibility that the sequence of CysA is modified.
2. -Authors are required to show MW of produced CysA produced from the WT and mutant Fungi.
3. -Authors are required to report that if the produced peptide is secreted by the irradiated fungus or is produced from its next generation. In the latter case, the work is significantly important.
4. -The details of employed instruments (LC/MS), and the obtained data as well, should be included in the MM and Results sections.
5. -Some figures labels are typed in Persian.
6. -Authors are required to provide suitable REFERENCE(S) for UV irradiations.
7. -Statistical-related issues like SEM/SD or triplicate/duplicates should be checked by an expert.
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Ref. Bio-synthesis, purification and structural analysis of Cyclosporine-A produced by Tolypocladium inflatum with valorization of agro-industrial wastes

Responses:

Thank you sincerely for your valuable comments. The answers and our revisions are as following:

1. Regarding *Tolypocladium inflatum* PTCC 5253, the strain was purchased from Iranian Research Organization for Science and Technology (IROST). The information is added in the text.
2. There was no difference between CyA mass (1202) produced by WT or mutant fungi. We applied an extracted-ion chromatogram (XIC) covering major positive adducts including proton adduct of CyA with an m/z value of 1203, and sodium adduct of CyA, with an m/z value of 1224. Further details are added in the text.
3. CyA was produced by the second passage of irradiated fungal strains, as they were cultured on a MYA plate after UV-irradiation and were evaluated for bioactivity, and

then the most active mutants were cultured on different MYA plates which in turn were used as a source of fermentation broth inoculation.

4. More details of LC/MS instrument and the applied protocol are added.
5. Figure 2 is corrected.
6. More relevant references are added.
7. Statistical analyses have been checked again.
8. The correlation is due to the increased biomass which leads to both elevated CyA production and medium viscosity. The requested reference is added.

The mentioned reference is added.

Associate Editor 1:

Dear Authors,

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Thank you for your contributions to the field, and we look forward to your revised submission.

Best regards,

E.I.C

Journal of Reports in Pharmaceutical Sciences

Responses:

Thank you so much for your consideration of our submitted article. We hope that the revised manuscript will respond to the requested corrections and meet your standards to be considered for the publication. Thanks again.

2 Revision 1

0 comments

No public comments in this round.