Gmail Rini Dwiastuti <rinidwiastuti83@gmail.com>

Journal of Biomolecular Structure & Dynamics - Account Created in Manuscript Central

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Balas Ke: TBSD-peerreview@journals.tandf.co.uk
Kepada: rini_dwi@usd.ac.id

05-Feb-2021

Dear Dr Rini Dwiastuti:

Welcome to Journal of Biomolecular Structure & Dynamics - Manuscript Central site for online submission and review.

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Journal of Biomolecular Structure & Dynamics Editorial Office
Log in to Remove This Account - https://mc.manuscriptcentral.com/jbsd?URL_MASK=a77baa7e275148ffbf585790eafd781a

Journal of Biomolecular Structure & Dynamics - Decision on Manuscript ID TBSD-2021-0257

Journal of Biomolecular Structure & Dynamics <onbehalfof@manuscriptcentral.com>

6 Maret 2021 pukul 07.47

Balas Ke: rhs07@albany.edu
Kepada: rini_dwi@usd.ac.id

05-Mar-2021

Dear Dr Dwiastuti:

Your manuscript entitled "In Silico Modeling and Empirical Study of 4-n-Butylresorcinol Nanoliposome Formulation", which you submitted to Journal of Biomolecular Structure & Dynamics, has been reviewed. The referee comments are included at the bottom of this letter.

The referee(s) would like to see some revisions made to your manuscript before publication. Therefore, I invite you to respond to the referee(s)' comments and revise your manuscript.

When you revise your manuscript please highlight the changes you make in the manuscript in yellow high light. Please also ensure that you submit a clean version using the file designation 'Manuscript with track changes removed.'

Please provide a reply to the referee comments; summarizing the changes you have made within the body of the manuscript in response to the referee comments, and any other response that you want the editor and the referees to note. You should submit it as a separate document along with manuscript files "Response to Decision Letter and Reviewer Comments". Upload this as the first document. You indicate in the space provided in the response box that a separate document has been uploaded.

The changes should be presented IN the revised paper, explaining the changes in the response document does not help the reader. The only manuscript that you upload should be the revised one with changes highlighted in yellow. Any other versions of the manuscript should not be uploaded.

To start the revision, please click on the link below:

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This will direct you to the first page of your revised manuscript. Please enter your responses to the comments made by the referee(s) in the space provided. You can use this space to document any changes you made to the original manuscript. Please be as specific as possible in your response to the referee(s).

This link will remain active until you have submitted your revised manuscript. If you begin a revision and intend to finish it at a later time, please note that your draft will appear in the “Revised Manuscripts in Draft” queue in your Author Center.

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to Journal of Biomolecular Structure & Dynamics, your revised manuscript should be uploaded by 04-May-2021. If it is not possible for you to submit your revision by this date, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to Journal of Biomolecular Structure & Dynamics and I look forward to receiving your revision.

Sincerely,

Professor Sarma
Editor in Chief, Journal of Biomolecular Structure & Dynamics
rhs07@albany.edu

Referee(s)' Comments to Author:

Referee: 1

Comments to the Author
Abstract:
Please mention which type of MD simulation was performed in your study.
It is confusing the way in which it is described how MD simulation assist in nanoliposome formulation .
Introduction
Page 3, line 70-77. This paragraph is part of the methodology? it is not clear why this paragraph is placed here. So, I recommend you to cite this text and showed some examples.
Page 3, line 79-80. please put the reference
Page 3, line 85-87. Page 4, line 96-970. You describe a study related to the field, however it is not clearly explained why is the relation with your study or why did you include this citation, please describe the relation with your study or why it was used as background.
Along the manuscript you mentioned molecular modeling, but the concept is employed under different scenarios, please clarify the concept because it is misused in some of them.
Page 4, line 103. it is advisable to mention the time of the application, because relatively in terms of clinical studies its is imprecise and it is not a common term.
Page 4, line 107-108. You mention that the stability is improved by encapsulating the compound, but is this a rule? Please add the reference.
Along the manuscript you mix terms like molecular modelling with Molecular dynamic simulations, and they are different tools of in silico studies. Please clarify the concepts and use them properly in the text.
I recommend you to rewrite your introduction because since my point of view you stat each paragragh with some lines of your work (metodology) followed by literature that support the the initial idea. it results very confusing to follow the idea that you want to transmit, it is very hard to understand the background of your work, besides I recommend you to add the reference where correspond because there are several ideas without references.
Material and methods
In section 2., GC-MS analysis, I suggest you to add a couple of line clarifiying why did you performed GC. Please also mention which is the ion source?
Why did you use GC and not other thectnique in ofrder to avoiod the thermal insability mentioned in the result section???
In section 3. Molecular dynamics simulation. I recommend you to menione how di you determine the composiion of the liposome at the beginning of the paragraph.
Please also give the number of water beads used.

Please clarify the temperature used in your smulation and experiments, because in MD section you mentioned that it was carried out at 323 K , and in the experimental section you say that you employed 500 °C, in kelvins it is 773.15 K.
Section 5. The conversion of soy lecitin
did you get the concentration of tthe phospholipids in your sistyem 387.12 mg/mL
Please review the calculation performed in the section five, since there are mistakes in the numbers.
Results
The potential energy calculation
the term "the number of potential energy" is not correct, please verify it.
page 10. the phrase "In contrast, the increase of the lipid number, the decrease of
244 the hydrogen bond in water", Please clarify the sentence because it is not clearly explained to what are you referring to.
Table 5. Please describe which type of energy is showed in this table.
Figure 1. Why are there four lines per graphic? please clarify
Figure 2. Please describe these graphs and what did you conclude about them?
Page 12. You write: The radius of gytation of nanoliposome was formed....
Please clarigy because the Rg was not formed, the nanoliposopme was formed and the Rg allow you to measure the nanoliposome formation.
I suggest you to be more descriptive about your MD simulation.
Figure 4. Why did you put a couple of figures per section. It would be better if you use boxes to separate these figures.
pag. 16, The phrase "structures were generated in the molecular
332 modeling simulation without the electrostatic energy", how did you omit the electrostatic energy?? Please clarify
It seems that the basis of molecular dynamic simulation are not clear, such as potential energy and the components of the same. Please review this concepts in order to improve the discussion of your results.

Referee: 2

Comments to the Author
Manuscript ID: TBSD-2021-0257

Reviewer´s comments:

The manuscript entitled “In Silico Modeling and Empirical Study of 4-n-Butylresorcinol Nanoliposome Formulation”, describes the molecular dynamics simulations of three lecithin systems with different numbers of molecules for liposome formation. One of these systems was prepared experimentally and it was confirmed that the theoretical and experimental liposome sizes coincide.

As a general comment, this article is relevant because using soy lecithin in liposomal formulations reduces costs considerably, compared to using pure phospholipids. The authors' proposal to carry out soy lecithin molecular dynamics (MD) experiments in order to predict the size of liposomes is a very good idea and improves the liposome formation methodology.
However, the authors do not discuss the differences or similarities of liposomes obtained by MD with and without 4-n-butylresorcinol (size, energy and shape). They only give the theoretical size of one of the systems, but it would be necessary to give the sizes of the 2 missing systems to verify if the difference is relevant or not and include some discussion. The manuscript can be accepted after addressing the following comments.

1. Page 1. Title: The author uses the word “Nanoliposom” instead of “Nanoliposome”. Please change.
2. Page 2 line 70: The information can be expanded by mentioning physicochemical parameters as size and zeta potential. They are important for the stability.
3. Page 4 line 94: The authors didn´t mention the results found by the aforementioned researchers.
4. Methodology: the authors must clarify if the liposome size reported is the radius or the diameter. It is desirable that they clearly explain how the liposome size is calculated from the radius of gyration.
5. Page 5 line 151: Concentration of 4-n- butylresorcinol was not given.
6. Page 6 line 172: the authors say that “The temperature in the formulation was selected at 500 °C ...” Please correct.
7. Page 7 line 200: The angle and the temperature used in the liposome size measurements are not given. It should be clarified if the size distribution was measured by intensity, number or volume, since choosing one of these parameters over the others give variations in size.
8. Figure 1 y 3: The authors didn´t explain why there are 2 blue lines and 2 two green lines. Please explain what each means. The chosen colors are difficult to distinguish.
9. Figure 4: Why they put two images for each system? Please clarify.
10. Table 6: Please add the liposome sizes found for all systems studied by MD. (2400 an 2800 are missing).
11. Figure 6: Specify the size of the scale bar in the caption of figure 6, since it is not visible in the photo. The authors should mention the diameter measurement of the liposomes shown in figure 6 by TEM.
12. The authors should include the liposome size distribution graphs obtained from the DLS, to see if there is a single population or not.
13. Do the number of drug molecules affects the liposome size?. Please clarify.
14. It is desirable that the authors perform the experiments with the 3200 system without drug in order to corroborate their MD results. Also mention how reproducible is their experimental procedure, it seems that they only made once the experiments.
15. Page 16 line 324: The authors say “It is also important to note that the slower liposome formation tends to give the phospholipid bilayer a chance to form a multiple connection, leading to an imperfect sphere or a bilayer bridge in the middle of the liposome.” Please mention the corresponding figures.
16. Page 17 line 374: The authors say “These insignificant results ….” I guess the authors didn´t mean insignificant, please verify. I´m not sure what do the authors mean by “deal”. Could you please clarify?

Referee: 3

Comments to the Author
1.The idea of the work is good but 80% of the work is based on computational analysis it lacks experimental evidence so requires a few experimental data to validate it

Editor's Comments to Author:

Associate Editor
Comments to Author:
(There are no comments.)

Gmail

Rini Dwiastuti <rinidwiastuti83@gmail.com>

Journal of Biomolecular Structure & Dynamics - Decision on Manuscript ID TBSD-2021-0257.R1

Journal of Biomolecular Structure & Dynamics <onbehalfof@manuscriptcentral.com>

11 Mei 2021 pukul 07.18

Balas Ke: rhs07@albany.edu
Kepada: rini_dwi@usd.ac.id

10-May-2021

Dear Dr Dwiastuti:

Your manuscript entitled "In Silico Modeling and Empirical Study of 4-n-Butylresorcinol Nanoliposome Formulation", which you submitted to Journal of Biomolecular Structure & Dynamics, has been reviewed. The referee comments are included at the bottom of this letter.

The reviews are in general favourable and suggest that, subject to minor revisions, your paper could be suitable for publication. Please consider these suggestions, and I look forward to receiving your revision.

When you revise your manuscript please highlight the changes you make in the manuscript by using yellow highlight. Please also ensure that you submit a clean version using the file designation 'Manuscript with track changes removed.'

Please provide a reply to the referee comments; summarizing the changes you have made within the body of the manuscript in response to the referee comments, and any other response that you want the editor and the referees to note. You should submit it as a separate document along with manuscript files "Response to Decision Letter and Reviewer Comments". Upload this as the first document. You indicate in the space provided in the response box that a separate document has been uploaded.

The changes should be presented IN the revised paper, explaining the changes in the response document does not help the reader. The only manuscript that you upload should be the revised one with changes highlighted in yellow. Any other versions of the manuscript should not be uploaded.

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This link will remain active until you have submitted your revised manuscript. If you begin a revision and intend to finish it at a later time, please note that your draft will appear in the “Revised Manuscripts in Draft” queue in your Author Center.

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to Journal of Biomolecular Structure & Dynamics, your revised manuscript should be uploaded by 09-Jun-2021. If it is not possible for you to submit your revision by this date, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to Journal of Biomolecular Structure & Dynamics and I look forward to receiving your revision.

Sincerely,
Professor Sarma
Editor in Chief, Journal of Biomolecular Structure & Dynamics

rhs07@albany.edu

Referee(s)' Comments to Author:

Referee: 1

Comments to the Author
The authors of the Manuscript "In Silico Modeling and Empirical Study of 4-n Butylresorcinol Nanoliposome Formulation" have given relevant explanation for all the queries given and the proper correction for all the types of typographical errors have been made . Necessary references were also included. Thus the manuscript can be accepted in your esteemed journal for publication.

Referee: 2

Comments to the Author
Major corrections were made but there are still some issues that shoul be corrected.
Abstract: You say: "using molecular dynamics simulation followed by potential energy calculation to understand the dynamics of the liposome assembly and the morphology". But the potential energy is not a parameter to study structural modifications, Rg give you the details that you mention above.

Please review the english and overall drafting of the manuscript.

5. conversion of soy lecithin frommolecular modelling: from where did you obtain the value: 100 nm?

the new reference does not have the same format than the original manuscript, please correct it.

Editor's Comments to Author:

Associate Editor
Comments to Author:
(There are no comments.)

Gmail

Rini Dwiastuti <rinidwiastuti83@gmail.com>

Journal of Biomolecular Structure & Dynamics - Decision on Manuscript ID TBSD-2021-0257.R2

Journal of Biomolecular Structure & Dynamics <onbehalfof@manuscriptcentral.com>

7 Juni 2021 pukul 22.36

Balas Ke: rhs07@albany.edu
Kepada: rini_dwi@usd.ac.id

07-Jun-2021

Dear Dr Dwiastuti:

Your manuscript entitled "In Silico Modeling and Empirical Study of 4-n-Butylresorcinol Nanoliposome Formulation", which you submitted to Journal of Biomolecular Structure & Dynamics, has been reviewed. The referee comments are included at the bottom of this letter.

The reviews are in general favourable and suggest that, subject to minor revisions, your paper could be suitable for publication. Please consider these suggestions, and I look forward to receiving your revision.

When you revise your manuscript please highlight the changes you make in the manuscript by using yellow highlight. Please also ensure that you submit a clean version using the file designation 'Manuscript with track changes removed.'

Please provide a reply to the referee comments; summarizing the changes you have made within the body of the manuscript in response to the referee comments, and any other response that you want the editor and the referees to note. You should submit it as a separate document along with manuscript files "Response to Decision Letter and Reviewer Comments". Upload this as the first document. You indicate in the space provided in the response box that a separate document has been uploaded.

The changes should be presented IN the revised paper, explaining the changes in the response document does not help the reader. The only manuscript that you upload should be the revised one with changes highlighted in yellow. Any other versions of the manuscript should not be uploaded.

To start the revision, please click on the link below:

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This will direct you to the first page of your revised manuscript. Please enter your responses to the comments made by the referee(s) in the space provided. You can use this space to document any changes you made to the original manuscript. Please be as specific as possible in your response to the referee(s).

This link will remain active until you have submitted your revised manuscript. If you begin a revision and intend to finish it at a later time, please note that your draft will appear in the “Revised Manuscripts in Draft” queue in your Author Center.

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to Journal of Biomolecular Structure & Dynamics, your revised manuscript should be uploaded by 07-Jul-2021. If it is not possible for you to submit your revision by this date, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to Journal of Biomolecular Structure & Dynamics and I look forward to receiving your revision.

Sincerely,
Professor Sarma
Editor in Chief, Journal of Biomolecular Structure & Dynamics

rhs07@albany.edu

Referee(s)' Comments to Author:

Referee: 1

Comments to the Author
The authors have improved the quality of the Manuscript and performed all the pertinent corrections. However, one last thing. You mention in the last revision: Thank you very for the suggestion. We have revised the statement as follow: "The in silico modeling was performed using molecular dynamics simulation followedby radius of gyration observation to understand the dynamics of the liposomeassembly and the morphology of the formed liposome (Line 29-32)". But after reviewing the manuscrip I observed tha it was not corrected. Please modify the statement as you mentioned before. After that I think that your manuscript will be ready for publication.

Editor's Comments to Author:

Associate Editor
Comments to Author:
(There are no comments.)

Gmail

Rini Dwiastuti <rinidwiastuti83@gmail.com>

Journal of Biomolecular Structure & Dynamics - Manuscript ID TBSD-2021-0257.R3 has been submitted online

Journal of Biomolecular Structure & Dynamics <onbehalfof@manuscriptcentral.com>

10 Juni 2021 pukul 13.24

Balas Ke: TBSD-peerreview@journals.tandf.co.uk
Kepada: rini_dwi@usd.ac.id

10-Jun-2021

Dear Dr Dwiastuti:

Your manuscript entitled "In Silico Modeling and Empirical Study of 4-n-Butylresorcinol Nanoliposome Formulation" has been successfully submitted online and is presently being given full consideration for publication in Journal of Biomolecular Structure & Dynamics.

Your manuscript ID is TBSD-2021-0257.R3.

Please mention the above manuscript ID in all future correspondence or when calling the office for questions. If there are any changes in your street address or e-mail address, please log in to ScholarOne Manuscripts at https://mc.manuscriptcentral.com/jbsd and edit your user information as appropriate.

You can also view the status of your manuscript at any time by checking your Author Center after logging in to https://mc.manuscriptcentral.com/jbsd.

If you do not hear from the editor within 2 months, please contact me.

Thank you for submitting your manuscript to Journal of Biomolecular Structure & Dynamics.

Sincerely,
Journal of Biomolecular Structure & Dynamics Editorial Office

Journal of Biomolecular Structure & Dynamics

Decision Letter (TBSD-2021-0257.R3)

From: rhs07@albany.edu

To: rini_dwi@usd.ac.id

CC:

Subject: Journal of Biomolecular Structure & Dynamics - Decision on Manuscript ID TBSD-2021-0257.R3

Body: 17-Jun-2021

Dear Dr Dwiastuti:

Ref: In Silico Modeling and Empirical Study of 4-n-Butylresorcinol Nanoliposome Formulation

Our referees have now considered your paper and have recommended publication in Journal of Biomolecular Structure & Dynamics. We are pleased to accept your paper in its current form which will now be forwarded to the publisher for copy editing and typesetting. The referee comments are included at the bottom of this letter, along with those of the editor who coordinated the review of your paper.

Within weeks, your paper will be published online ahead of print as a 'Latest Article', which can be cited using the DOI.

You will receive proofs for checking, and instructions for transfer of copyright in due course.

The publisher also requests that proofs are checked through the publisher's tracking system and returned within 48 hours of receipt.

If you have any questions about the status of your manuscript, please contact the Journal Editorial Office (TBSD-peerreview@journals.tandf.co.uk).

Thank you for your contribution to Journal of Biomolecular Structure & Dynamics and we look forward to receiving further submissions from you.

Sincerely,
Professor Sarma
Editor in Chief, Journal of Biomolecular Structure & Dynamics
rhs07@albany.edu

Referee(s)' Comments to Author:

Editor's Comments to Author:

Associate Editor
Comments to Author:
(There are no comments.)

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Date Sent: 17-Jun-2021