andang miatmoko <andang-m@ff.unair.ac.id>

Scientific Reports: Decision on your manuscript

4 messages

Scientific Reports <srep@nature.com> Tue, Dec 27, 2022 at 8:20 PM
To: andang-m@ff.unair.ac.id

Ref: Submission ID cdf48bd0-0dc3-4db5-96f2-4bfd93589444

Dear Dr Miatmoko,

Re: "The Effect of 1,2-Dioleoyl-3-Trimethylammonium Propane (DOTAP) Addition on the Physical Characteristics of β-Ionone Liposomes"

We are pleased to let you know that your manuscript has now passed through the review stage and is ready for revision. Many manuscripts require a round of revisions, so this is a normal but important stage of the editorial process.

Editor comments
Please address all the 3 reviewers' comments.

To ensure the Editor and Reviewers will be able to recommend that your revised manuscript is accepted, please pay careful attention to each of the comments that have been pasted underneath this email. This way we can avoid future rounds of clarifications and revisions, moving swiftly to a decision.

Once you have addressed each comment and completed each step listed below, the revised submission and final file can be uploaded via the link below.

If you completed the initial submission, please log in using the same email address. If you did not complete the initial submission, please discuss with the submitting author, who will be able to access the link and resubmit.

https://submission.springernature.com/submit-revision/cdf48bd0-0dc3-4db5-96f2-4bfd93589444

You can visit https://researcher.nature.com/your-submissions to track progress of this or any other submissions you might have.

CHECKLIST FOR SUBMITTING YOUR REVISION

1. Please upload a point-by-point response to the comments, including a description of any additional experiments that were carried out and a detailed rebuttal of any criticisms or requested revisions that you disagreed with. This must be uploaded as a 'Point-by-point response to reviewers' file.

You'll find a handy one-page PDF on how to respond to reviewers' comments here:

https://www.nature.com/documents/Effective_Response_To_Reviewers-1.pdf

2. Please highlight all the amends on your manuscript or indicate them by using tracked changes.

3. Check the format for revised manuscripts in our submission guidelines, making sure you pay particular attention to the figure resolution requirements:

https://www.nature.com/srep/publish/guidelines

Finally, if you have been asked to improve the language or presentation of your manuscript and would like the assistance of paid editing services, then our expert help at Springer Nature Author Services can help you improve your manuscript through services including English language editing, developmental comments, manuscript formatting, figure preparation, translation, and more.

To find out more and get 15% off your order then click the link below.

https://authorservices.springernature.com/go/sn/?utm_source=SNAPP&utm_medium=Revision+Email&utm_campaign=SNAS+Referrals+2022&utm_id=ref2022

Please note that use of an editing service is neither a requirement nor a guarantee of publication. Free assistance is available from our resources page: https://www.springernature.com/gp/researchers/campaigns/english-language-forauthors

To support the continuity of the peer review process, we recommend returning your manuscript to us within 14 days. If you think you will need additional time, please let us know and we will aim to respond within 48 hours.

Kind regards,

Arezoo Sodagar Taleghani
Editorial Board Member
Scientific Reports

Reviewer Comments:

Reviewer 1
1. In the introduction, before doing the literature survey of DOTAP, introduce what DOTAP is in one to two lines. Also, it is not required to add this much of literature survey for DOTAP, but make it more concise.
2. Line 81, Cationic lipid 17, 17 should be a superscript.
3. Line 123 the effect of the addition of different levels of DOTA, (typo, should be DOTAP).
4. Lines 89-96 the authors mentioned that in the literature the sizes reduced with increasing the concentration of DOTAP. while in their work the addition of DOTAP increases the size of liposomes (line 130), why is it contradicting to the literature?
5. Lipo-DOTAP blank and ION-DOTAP 3 are having the same concentration of DOTAP, and their sizes are similar, so the statement “However, the size decreased with the addition of β-ionone to the formula, as shown in Figure 1A.” (line131-132), is not true. The size reduced because of the low concentration of DOTAP and not due to the addition of β-ionone.
6. Figure 1 is not a histogram, but a bar graph. The comparison is between Lipo-blank to the others.
7. Figure 3 is spectra is not properly visible.
8. Line 209, it is 214 C and not 124 C
9. From Calcein release studies - Increasing the DOTAP concentration reduced the stability of liposomes, which is not a positive feature.
10. The fluorescent images are not at the acceptable quality. Although the authors mentioned an increase in fluorescence, it appears that it is due to the increase in exposure time, the same increase in brightness can be seen in the bright field images as well for the Lipo-DOTAP-Blank and DOTAP-3. From figure 8, Lipo-DOTAP-Blank has the least amount of Coumarin-6, since both Lipo-DOTAP-Blank and ION-DOTAP-3 has the same amount of DOTAP, why is there a difference in Coumarin-6 intake by the cells, also this result contradicts to the fluorescent image in the figure 7.
11. “Preparation Of β-Ionone Liposomes Containing Coumarin-6 as the Fluorescent Labelling Agent” The component ratio of the liposome prepared is entirely different from what is mentioned in table 2. The mole ratio between HSPC:β-Ionone:Cholesterol:DSPE-PEG:DOTAP is 35:140:70:5:6. Again, the concentrations of lipids are too high, which might be the reason why they obtained multilamellar liposomes.
12. In the conclusion, the authors said that incorporation of DOTAP improved the liposome formulation for cancer therapy, but, it is not convincing from the results. Although β-Ionone was encapsulated, no studies were done to signify its effects, no cell viability studies, encapsulation efficiency etc. Furthermore, addition of DOTAP made the liposomes multilamellar, reduced the stability and it does not appear to have improved the cellular intake.

Reviewer 2
Comments to the Authors
This manuscript investigates that the effects of DOTAP addition on the physical characteristics of β-Ionone liposomes. This work reported that the addition of DOTAP to β-ionone liposomes made the liposomes positively charged and increased particle size, membrane fluidity, and intracellular uptake. The experiments are well designed and results are mostly credible. However, there are still some problems that need to be clarified.
1. The author found that DOTAP, as one of the widely used cationic liposome materials in recent years, can reduce particle size, increase membrane fluidity and increase cell uptake through literature research. So what is the innovation of this study?
2. The conclusions obtained in this paper are the same as the results of the literature survey. Is your research meaningful?
3. The notes in Figure 4 are the same as those in Figure 3. Please check them carefully.
4. Does line 238 refer to Table 2? Please confirm.
5. The author mentioned that β-ionone and DOTAP have certain effects on lung. Why did HeLa cells be selected as the research object?
6. In order to make the results more convincing, it is suggested to increase the quantitative analysis of fluorescence intensity in the cellular uptake of β-ionone liposomes.
7. The discussion section should be more in-depth.
8. It is mentioned in the experimental method that the polydispersion index is measured, but there is no result of this

part. Please explain.
9. In the experimental methods section, evaluation of vesicle morphology of β-Ionone liposomes using TEM was repeated. Please check it carefully.

Reviewer 3
The article is interesting, and deserves publication in the journal after some revision:
1. Table 2. from MATERIALS AND METHODS should be moved to RESULTS because it is not clear which liposomes are being discussed.
2. What the hydrodynamic diameter is given in fig. 1? Averaged over intensity or number of particles?
3. Why is there a slight decrease after the maximum in the calcein release curves in Fig. 6? For example, at 8 hours for ION-DOTAP 1 and ION-DOTAP 2 systems, at 4 hours - for ION-DOTAP 3.
4. What is the encapsulation efficiency of calcein? Could this have affected the release profiles?
5. For publication in such a journal, it is not enough to conduct research on a model substrate. It is necessary to load an anticancer drug, for example, doxorubicin, into the developed systems and study the change in its cytotoxicity when encapsulated in liposomes.
6. Why was this cell line chosen?
7. Why is this β-ionone molar ratio chosen? Have other molar ratios been tested?

Lots of misprints. Authors should carefully read their manuscript. For example:
1. Lines 49-50: «in lung cancer cell death, (A549) through» replace with «in lung cancer cell (A549) death, through»;
2. Line 79: «Cationic lipid 17» replace with «Cationic lipid17»;
3. Line 103: link is incorrectly formatted «(Wang et al., 2012)»;
4. Line 120: «DOTA» replace with «DOTAP»;
5. Line 215: the section name is given twice;
6. Lines 266-267: «DOTAP, a cationic phospholipid containing an NH4+ group, is low in toxicity compared to other cationic lipids18.». Exactly the same sentence was given in the introduction (lines 80-82). Remove duplication;
7. Calcein sometimes writes with a small letter, sometimes with a capital letter. Bring everything to the same view.

Andang MIATMOKO <andang-m@ff.unair.ac.id> Thu, Jan 12, 2023 at 5:47 PM
To: Scientific Reports <srep@nature.com>

Dear Editor,
Could you please give us an extension to submit the revision for about 2-3 weeks? Since there was an end of year holiday, we needed to arrange the revision appropriately.
Many thanks
[Quoted text hidden]
--
Salam,

Andang Miatmoko, PhD., Apt.
Department of Pharmaceutical Sciences
Faculty of Pharmacy, Airlangga University
Nanizar Zaman Joenoes Building
Campus C Airlangga University, Mulyorejo, 60115
Surabaya

Pooja Bisht <srep@nature.com> Fri, Jan 13, 2023 at 12:15 PM
Reply-To: Pooja Bisht <srep@nature.com>
To: andang-m@ff.unair.ac.id

Dear Dr. Miatmoko,

Thank you for your email.

This will not be a problem – we do appreciate that some revisions do take longer than others and we would be more than happy to accommodate an extension for you till 31 Jan 2023.

Please submit your revised manuscript when you are ready.

Best Regards,

Pooja Bisht
Editorial Support at Scientific Reports

> On Thu, 12 Jan at 10:47 AM , Andang-m <andang-m@ff.unair.ac.id> wrote:
> **[External - Use Caution]**
> [Quoted text hidden]

Pooja Bisht <srep@nature.com> Fri, Feb 10, 2023 at 11:35 PM
Reply-To: Pooja Bisht <srep@nature.com>
To: andang-m@ff.unair.ac.id

Dear Dr. Miatmoko,

Hope this email finds you well.

As per your request we grant you further extension till 24 Feb 2023.

Please submit your revised manuscript when you are ready.

Best Regards,
Pooja Bisht
Editorial Support at Scientific Reports

> On Fri, 13 Jan at 5:15 AM , Pooja Bisht <srep@nature.com> wrote:
> Dear Dr. Miatmoko,
>
> Thank you for your email.
>
> This will not be a problem – we do appreciate that some revisions do take longer than others and we would be more than happy to accommodate an extension for you till 31 Jan 2023.
>
> Please submit your revised manuscript when you are ready.
>
> Best Regards,
> **Pooja Bisht**
> Editorial Support at Scientific Reports
>
> > On Thu, 12 Jan at 10:47 AM , Andang-m <andang-m@ff.unair.ac.id> wrote:
> > **[External - Use Caution]**
> > [Quoted text hidden]

andang miatmoko <andang-m@ff.unair.ac.id>

Scientific Reports: Decision on your manuscript

1 message

Scientific Reports <srep@nature.com> Fri, Mar 3, 2023 at 9:07 PM
To: andang-m@ff.unair.ac.id

Ref: Submission ID cdf48bd0-0dc3-4db5-96f2-4bfd93589444

Dear Dr Miatmoko,

Re: "The Effect of 1,2-Dioleoyl-3-Trimethylammonium Propane (DOTAP) Addition on the Physical Characteristics of β-Ionone Liposomes"

We are pleased to let you know that your manuscript has now passed through the review stage and is ready for revision. Many manuscripts require a round of revisions, so this is a normal but important stage of the editorial process.

Editor comments
Please revise your manuscript based on the reviewer's comments.

To ensure the Editor and Reviewers will be able to recommend that your revised manuscript is accepted, please pay careful attention to each of the comments that have been pasted underneath this email. This way we can avoid future rounds of clarifications and revisions, moving swiftly to a decision.

Once you have addressed each comment and completed each step listed below, the revised submission and final file can be uploaded via the link below.

If you completed the initial submission, please log in using the same email address. If you did not complete the initial submission, please discuss with the submitting author, who will be able to access the link and resubmit.

https://submission.springernature.com/submit-revision/cdf48bd0-0dc3-4db5-96f2-4bfd93589444

You can visit https://researcher.nature.com/your-submissions to track progress of this or any other submissions you might have.

CHECKLIST FOR SUBMITTING YOUR REVISION

1. Please upload a point-by-point response to the comments, including a description of any additional experiments that were carried out and a detailed rebuttal of any criticisms or requested revisions that you disagreed with. This must be uploaded as a 'Point-by-point response to reviewers' file.

You'll find a handy one-page PDF on how to respond to reviewers' comments here:

https://www.nature.com/documents/Effective_Response_To_Reviewers-1.pdf

2. Please highlight all the amends on your manuscript or indicate them by using tracked changes.

3. Check the format for revised manuscripts in our submission guidelines, making sure you pay particular attention to the figure resolution requirements:

https://www.nature.com/srep/publish/guidelines

Finally, if you have been asked to improve the language or presentation of your manuscript and would like the assistance of paid editing services, then our expert help at Springer Nature Author Services can help you improve your manuscript through services including English language editing, developmental comments, manuscript formatting, figure preparation, translation, and more.

To find out more and get 15% off your order then click the link below.

https://authorservices.springernature.com/go/sn/?utm_source=SNAPP&utm_medium=Revision+Email&utm_campaign=SNAS+Referrals+2022&utm_id=ref2022

Please note that use of an editing service is neither a requirement nor a guarantee of publication. Free assistance is available from our resources page: https://www.springernature.com/gp/researchers/campaigns/english-language-forauthors

To support the continuity of the peer review process, we recommend returning your manuscript to us within 14 days. If you think you will need additional time, please let us know and we will aim to respond within 48 hours.

Kind regards,

Arezoo Sodagar Taleghani
Editorial Board Member
Scientific Reports

Reviewer Comments:

Reviewer 3
I am satisfied with the work that the authors have done to correct all my comments and answer my questions.

Reviewer 1
There are some concerns in the revision

Line 18 efficiency1817 , check the citation style

Line 470 Liposomes were prepared according to the formula in the Table 2 by adding Coumarin-6 to each mL of liposomes. Please mention the amount of Coumarin-6 added.

Line 482 1x 107 cells per mL is too high for a 6 well plate.

Line 484-485 The medium was replaced with β-ionone liposomes at a coumarin-6 concentration of 10g/mL. The concentration 10g/ml, is that correct?

Line 132 "However, the size decreased with the addition of DOTAP to the formula, as shown in Figure 1.A", From figure 1 A, the size increased with the addition of DOTAP.

For the commend no 10, “Since both Lipo-DOTAP-Blank and ION-DOTAP-3 have the same amount of DOTAP, why is there a difference in Coumarin-6 intake by the cells”
The response was. “LIPO-DOTAP-Blank has a high deviation, probably because the presence of beta-ionone affects it.” However, from the figure, the deviation is not high and LIPO-DOTAP-Blank does not have beta-ionone. LIPO-DOTAP-Blank is the second bar in the graph, and it has a low error bar.

Line 274-275 The results showed that there is an increase in cytotoxicity of the ION-DOXO-DOTAP-2 formula in T47D cells (Fig. 9B). There is a mismatch between the statement and the figure 9 description where its written 9.B is Hela and 9C is T47D.

The IC 50 values from 9.C should be much less than 1 µg/ml and ION-DOXO-DOTAP 0 and ION-DOXO- DOTAP 2 should have similar IC 50 values.

Reviewer 2
The authors have responded well to the reviewers' comments, and the manuscript is ready for publication

andang miatmoko <andang-m@ff.unair.ac.id>

Scientific Reports: Decision on your manuscript

1 message

Scientific Reports <srep@nature.com> Tue, Mar 14, 2023 at 1:11 PM
To: andang-m@ff.unair.ac.id

Ref: Submission ID cdf48bd0-0dc3-4db5-96f2-4bfd93589444

Dear Dr Miatmoko,

Re: “The Effect of 1,2-Dioleoyl-3-Trimethylammonium Propane (DOTAP) Addition on the Physical Characteristics of β-Ionone Liposomes”

We’re delighted to let you know your manuscript has now been accepted for publication in Scientific Reports.

Editor comments
The final decision: Accept

Licence to Publish and Article Processing Charge

As the corresponding author of an accepted manuscript, your next steps will be to complete an Open Access Licence to publish on behalf of all authors, confirm your institutional affiliation, and arrange payment of your article-processing charge (APC). You will shortly receive an email with more information.

Checking the proofs

Prior to publication, our production team will also check the format of your manuscript to ensure that it conforms to the standards of the journal. They will be in touch shortly to request any necessary changes, or to confirm that none are needed.

Once we've prepared your paper for publication, you will receive a proof. At this stage, please check that the author list and affiliations are correct. For the main text, only errors that have been introduced during the production process, or those that directly compromise the scientific integrity of the paper, may be corrected.

Please make sure that only one author communicates with us and that only one set of corrections is returned. As the corresponding (or nominated) author, you are responsible for the accuracy of all content, including spelling of names and current affiliations.

To ensure prompt publication, your proofs should be returned within two working days.

Publication is typically within two weeks of the proofs being returned. Please note there will be no further correspondence about your publication date. When your article is published, you will receive a notification email. If you are planning a press release, contact scirep.production@springernature.com when you receive the proofs to arrange a specific publication date.

Publication policies

Acceptance of your manuscript is conditional on all authors agreeing to our publication policies at: https://www.nature.com/srep/journal-policies/editorial-policies.

Your article will be open for online commenting on the Scientific Reports website. Please use the report facility if you see any inappropriate comments, and of course, you can contribute to discussions yourself. If you wish to track comments on your article, please register by visiting the 'Comments' section in the full text (HTML) version of your paper.

A form to order reprints of your article is available at https://www.nature.com/reprints/author-reprints.html. To obtain the special author reprint rate, orders must be made within a month of the publication date. After that, reprints are charged at the normal (commercial) rate.

Once again, thank you for choosing Scientific Reports, and we look forward to publishing your article.

Kind regards,

Arezoo Sodagar Taleghani
Editorial Board Member
Scientific Reports

Reviewer Comments:

Reviewer 1
The responses are satisfactory and the article can be published.

P.S. If appropriate, you may also consider uploading any protocols used in this manuscript to the protocol exchange, part of our online web resource, https://protocolexchange.researchsquare.com. By participating, you are enabling researchers to reproduce or adapt your methodology. The protocol exchange is fully searchable, providing your protocols and paper with increased utility and visibility. Protocols can also be easily updated via versioning. Please submit your protocol to https://protocolexchange.researchsquare.com/submission. You may need to create a new Research Square account. Please provide details of this article in the associated publications section. You'll find more information at: https://protocolexchange.researchsquare.com

** Visit the Springer Nature Editorial and Publishing website at www.springernature.com/editorial-and-publishing-jobs for more information about our career opportunities. If you have any questions, please email Editorial.Publishing.Jobs@springernature.com. **

This is a new page that we are continually improving.
We would love to hear your feedback and suggestions.

SPRINGER NATURE SNAPP

Scientific Reports scientific reports

My account

The Effect of 1,2-Dioleoyl-3-Trimethylammonium Propane (DOTAP) Addition on the Physical Characteristics of β-Ionone Liposomes

Current status

We've sent your submission to production

Our production department will be in touch with your proofs within 2 weeks of receiving your submission. They will email andang-m@ff.unair.ac.id with all further updates.

Progress so far

Progress so far

1. Submission received - complete
2. Initial technical check - complete
3. Peer review - complete
4. Submission accepted - complete
5. Publishing and rights - complete
6. Production - in progress

Your submission

Your submission

Title

The Effect of 1,2-Dioleoyl-3-Trimethylammonium Propane (DOTAP) Addition on the Physical Characteristics of β-Ionone Liposomes

Type

Article

Journal

Scientific Reports

Submission ID

cdf48bd0-0dc3-4db5-96f2-4bfd93589444

Need help?

If you have any questions about this submission, you can email the Editorial Office.

For general enquiries, please look at our support information.

Submission history

1. **Publishing and rights**

Submission status	Date
Publishing and rights complete	14 Mar 2023
Submission is in publishing and rights	14 Mar 2023

2. **Peer review**

Submission status	Date

Submission accepted	14 Mar 2023
Submission under peer review	09 Mar 2023
Submission passed technical check	09 Mar 2023
Revision received	07 Mar 2023
Submission under peer review	15 Feb 2023
Submission passed technical check	15 Feb 2023
Amendment received	14 Feb 2023
Revision received	13 Feb 2023
Submission under peer review	28 Sep 2022

3. Technical check

Submission status	Date
Submission passed technical check	28 Sep 2022
Amendment received	28 Sep 2022
Submission is under technical check	27 Sep 2022

4. Submission received

Submission status	Date
Submission received	27 Sep 2022