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OPEN PEER REVIEW

Preparation and in Vitro Property Research of Cholic Acid Nanoparticles with Dual-functions of Hemostasis and Antibacterial

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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

2 comments · 13 Feb 2023 – 4 Apr 2023

Referee 1 Reviewer

MINOR REVISION 13 Feb 2023

The authors presented interesting research on the antibacterial and hemostatic effects of the proposed nanoparticles. The materials seem to be available and inexpensive. The various hemorrhage models offered for in vivo evaluations were among the attractive points of this work. However, minor revision is suggested to ensure a more thorough research article:

1. Some more characterization tests are required for the nanoparticles, such as FTIR and XRD. An in vitro release test in phosphate-buffered saline can also be of assistance in understanding the performance of the nanoparticles in the bloodstream.
2. Cellular uptake studies can be of significance in determining the mechanism of this drug delivery system. The data from the uptake test can be used along with the aggregation studies to form more meaningful results.
3. The antibacterial capability of CDCA-PLL NPs was tested using the minimum inhibitory concentration (MIC) of PLL. Although the test produced promising results, it would have been meaningful to try CDCA-PLL NPs with smaller amounts of PLL (less than MIC). This could be beneficial in identifying the possible potentiation effect between CDCA and PLL and therefore providing an additional advantage for the co-administration of the two materials in a single nanoparticle.
4. It is good to consider the application of a physical mixture of CDCA and PLL as a control in some of the tests.
5. There are some grammatical issues that need to be checked, such as "to develop" in line 27, "due to PLL is rich in cations" in line 35 (both in the introduction section), and some other instances. These grammatical mistakes also need to be corrected.

Associate Editor

MINOR REVISION 4 Apr 2023

The reviewers' comments should be properly addressed.

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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.

Letter to Editor and Reviewers

Dear editor and reviewers,

Thank you very much for giving us such a precious opportunity to revise our manuscript entitled “Preparation and in vitro property research of cholic acid nanoparticles with dual functions of hemostasis and antibacterial” (ID: 135437) that has been submitted to Iranian Journal of Pharmaceutical Research. Both the editor and reviewers proposed some valuable comments which helped us markedly improve the quality of our submission. According to these suggestions and comments, revisions were made in our revised manuscript, the revised parts are marked in red. Our point-by-point responses to the original reviewers’ comments are provided in the Response to reviewers.

We would greatly appreciate your consideration of the revised manuscript for publication. We look forward to hearing from you.

Sincerely yours,
Dechuan Zhang, Senior Engineer ,
Department of Radiology, Chongqing Traditional Chinese Medicine Hospital, Chongqing 400021, China,

Response to Reviewers’ comments

Reviewer 1:
The authors presented interesting research on antibacterial and hemostasis effects of the proposed nanoparticles. The materials seem to be available and inexpensive. The various hemorrhage models offered for in vivo evaluations was among the attractive points of this work. However, minor revision is suggested to ensure a more thorough research article:

1. Some more characterization tests are required for the nanoparticles, such as FTIR and XRD. In vitro release test in phosphate buffer saline can also be of assistance in understanding the performance of the nanoparticles in the blood stream.

Reply: Thanks for your advices, which are really helpful for us to improve our article. We added the FT-IR test and in vitro release experiments in the revised manuscript.

2. Cellular uptake studies can be of significance in determining the mechanism of this drug delivery system. The data from the uptake test can be used along with the aggregation studies to form more meaningful results.

Reply: Thanks for your advices, Since nanoparticles we prepared are designed to be administrated locally and exert local pharmacological effects, we studied the mechanism of blood coagulation at the cellular level, and did not conduct cell uptake experiments.

3. Antibacterial capability of CDCA-PLL NPs was tested using the minimum inhibitory concentration (MIC) of PLL. Although the test produced promising results, it would have been meaningful to try CDCA-PLL NPs with fewer amounts of PLL (less than MIC). This could show benefit in finding out the possible potentiation effect between CDCA and PLL and therefore providing more advantage for the co-administration of the two materials in a single nanoparticle.

Reply: Thanks for your advices, we measured antibacterial capabilities of lower concentrations of PLL, CDCA and CDCA-PLL NPs and found CDCA-PLL NPs showed the best antibacterial effect. We revised the results in the manuscript.

4. It is good to consider application of CDCA and PLL physical mixture in some of the tests as a control.

Reply: Thanks for your suggestion. We used CDCA and PLL physical mixture as a control in the hemolytic test and found that the physical mixture showed almost the same hemolysis effect with PLL.

5. There are some grammatical issues that need to be checked; such as "to develop" in line 27,"due to PLL is rich in cations" in line 35 (both in introduction section), and some more points. These grammatical mistakes also need to be corrected.

Reply: Thanks for your suggestion. We are sorry for the grammatical issues in the text. We have made revision in the revised manuscript.

Reviewer 2:
Dear colleague;
generally, text of article is clear and correct. but there are some points about manuscript:
1.About title, however that "preparation" reflect the content of article correctly, but use of "property research" is very general. its better that you mention different type of experiment (in vitro or in vivo) that you did.

Reply: Thanks for your suggestion. We have revised the title into “Preparation and in vitro property research of cholic acid nanoparticles with dual functions of hemostasis and antibacterial”.

2.The different parts of abstract (introduction, method and material, result, conclusion) does not separate from each other and it causes some part of abstract shorter than other part. mainly of abstract describe result and positive points of experiment.

Reply: Thanks for your suggestion. We have revised the abstract with separate parts including objective, methods, results and conclusion in the revised manuscript.

3.In the introduction, hypothesis is clear. but general road map of experiment is not clear. you can add answer of this question to last paragraph of introduction :

-for characterization of nanoparticle, what tests you did?
-for evaluate of antibacterial effects, what tests you did?
you can use from other similar experiment and compare your rationales for choosing of tests with other experiments.

Reply: Thanks for your suggestion which is really useful to improve the quality of our work. We have added the contents in the introduction.

4.You did not describe the rationale of some choices. for example in biosafety evaluation, why did you use 540nm?

Reply: Thanks for your suggestion. We use 540nm in biosafety evaluation because red blood cells rupture has the best ultraviolet absorption at 540nm.

5.In characterization of nanoparticle, you can do an IR test before and after of nanoparticle forming. this spectrums can help you in detect of new bonds.

Reply: Thanks for your advices, which are really helpful for us to improve our article. We added the relevant experiments in the revised manuscript.

6.How do you separate the residual DMSO? and how do you assure that separate DMSO absolutely?

Reply: Thanks for your suggestion. The nanoparticles were prepared by dialysis, the residual DMSO can be separated in the process. Since DMSO is miscible with water, after dialysis in deionized water for 8 hours, the DMSO can be considered to be removed from the system.

7.How do you separate the residual CDCA? and how do you assure that separate CDCA absolutely?

Reply: Thanks for your suggestion. We separated the residual CDCA by dialysis, we lyophilized the nanoparticles to detect the drug content in CDCA-PLL NPs, which proved that the residual CDCA was separated.

8.In some sentences, you mention to "HDCA". what is the meaning of this abbreviation ? please revise manuscript and correct this points.

Reply: Thanks for your comments, we are sorry that “HDCA” are typing errors, we have revised the mistakes in the revised manuscript.

thanks for your attention.
with regards.

2 Revision 1

0 comments

No public comments in this round.

3

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.

Letter to Editor and Reviewers

Dear editor and reviewers,

Thank you for your precious comments on our manuscript entitled “Preparation and in vitro property research of cholic acid nanoparticles with dual functions of hemostasis and antibacterial” (ID: 135437) that has been submitted to Iranian Journal of Pharmaceutical Research. According to these suggestions and comments, revisions were made in our revised manuscript, the revised parts are marked in red. Our point-by-point responses to the original reviewers’ comments are provided in the Response to reviewers’ comments.

We would greatly appreciate your consideration of the revised manuscript for publication. We look forward to hearing from you.

Sincerely yours,

Dechuan Zhang, Senior Engineer ,
Department of Radiology, Chongqing Traditional Chinese Medicine Hospital, Chongqing 400021, China,

Response to Reviewers' comments

Dear author

Thanks for your attention to my comments and your revised.

Please check many points:

1.During preparation of sample for HPLC test, does drug loading capacity or encapsulation efficiency change? Can you demonstrate that it does not change?

Reply: Thanks for your comments. The samples for HPLC test are prepared by lyophilization, and CDCA was then dissolved in methanol and detected. The lyophilization process aims at removing water and other solvents, which may not change the constituent of nanoparticles.

2.About particle size, zeta potential and TEM picture its better that you compared PLL, CDCA and prepared nanoparticle.

Reply: Thanks for your advice. It would be better to compare PLL, CDCA and nanoparticles as you suggested. However, the PLL and CDCA alone could not form nanoparticles and corresponding tests could not be conducted.

3.Please write the caption of figure in detail and with more precision.

Reply: Thanks for your suggestion. We have rewritten the captions of figures in detail in the revised manuscript.

4.you had not the group of negative control in animal test. Can you explain about it?

Reply: Thanks for your suggestion. We used saline as negative control in animal test.

5.In conclusion part, its better that you indicate challenges that you had in way of your research. Also indicate weak points or features that need for more evaluation.

Reply: Thanks for your suggestion. We have added the contents in the revised manuscript.

6.What ideas are there for other researcher in this research? Please add your ideas in the end of conclusion.

Reply: Thanks for your comments. We have spoken at length with other researchers, and they confirmed the conclusions drawn in our article and suggested that CDCA-PLL NPs could be tested in more disease models to broaden its clinical application. We have added this part in the revised manuscript.

7.please add your answer to question 4,6,7 in last review letter to manuscript briefly.

Reply: Thanks for your suggestion which is really useful to improve the quality of our work. We have revised the manuscript according to your suggestions.

3 Revision 2

0 comments

No public comments in this round.