Iranian Journal of Pharmaceutical Research
Volume 22 · Issue 1 · e137011

OPEN PEER REVIEW

Solubility of Some Drugs in Aqueous Solutions of Choline Chloride-Based Deep Eutectic Solvent Systems: Experimental Data, Modeling, and the Impact of Solution pH

Samira Zadali Asghar, Raha Kaviani, Ali Shayanfar

SUBMITTED	REVISED	ACCEPTED	DOI
19 Apr 2023	21 May 2023	25 May 2023	10.5812/ijpr-137011

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.

More about open peer review: brieflands.com/knowledgebase/opr

Contents

1 **Original submission** Referee 1, Associate Editor, Referee 2, Editor-in-Chief 2
2 **Revision 1** Associate Editor, Editor-in-Chief 4
Authors' reply to reviewers 5
Reviewer and editor comments 8

1 Original submission

5 comments · 30 Apr 2023 – 15 May 2023

Referee 1 Reviewer

REJECT 30 Apr 2023

Dear AE,
This manuscript entitled “Solubility of Some Drugs in Aqueous Solution of Choline Chloride-Based Deep Eutectic Solvent (DES) System: Experimental Data, Modeling and the Effect of Solution pH” does not have enough novelty for publication in IJPR. The experimental section (solubility measurement) is too limited and the QSPR model is weak for publication. A Choline Chloride-Based solvent was used as a Deep Eutectic Solvent (DES) System in previous research. I recommended that this article be referred to a journal related to computational methods.

Associate Editor

REJECT 2 May 2023

Dear EIC,

Based on the reviewer's comment, rejection is recommended.
Regards,

Referee 2 Reviewer

MAJOR REVISION 15 May 2023

Dear AE,

The manuscript entitled “Solubility of Some Drugs in Aqueous Solution of Choline Chloride Based Deep Eutectic Solvent (DES) System: Experimental Data, Modeling and the Effect of Solution pH” is focused on the solubility studies of poorly water-soluble drugs in aqueous solutions of DES.
The topic of the article is within the scope of the journal, but there are some major revisions that should be addressed.
1. There are several studies regarding the advantages of DESs as alternative solvents for poorly soluble compounds. Solubility enhancement of various APIs in choline chloride-urea and choline chloride-glycerol has also been reported in the literature. Therefore, it is suggested that the novelty and significance of the study be clarified in the “Introduction”.
2. Due to the instability of this type of DES in the presence of water, how appropriate was its use in this study?
3. Why were the solubility measurements carried out at 37 °C rather than at room temperature?
4. Comparing the solubility of the APIs in DESs with their solubility in a conventional pharmaceutical solvent is suggested.
5. More details are required for the experimental section.
6. Table 2: The footnote should be corrected (a, b, …).
7. The conclusion should be improved considering the outcome of the research.
8. In general, the writing needs to be improved.

Associate Editor

MAJOR REVISION 15 May 2023

Dear Author,
Your article has been reviewed carefully by the reviewers. According to their comments, this document needs major revision. Please follow their comments as requested.
Thanks

Editor-in-Chief

MAJOR REVISION 15 May 2023

Dear Author,

Your manuscript needs some major revisions. The novelty and significance of the study should be clarified.
Thanks,

2

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.

20 May 2023
Dear Editor
Many thanks for your and the reviewer comments on our manuscript entitled: “Solubility of Some Drugs in Aqueous Solution of Choline Chloride-Based Deep Eutectic Solvent (DES) System: Experimental Data, Modeling and the Effect of Solution pH” with the manuscript ID 137011. We appreciate helpful suggestions to improve quality of the manuscript. After careful consideration, we have responded below to each of the comments. Additions to the text have been highlighted in the revised manuscript.

Best Regards
A.Sh.

Reviewer 1:
This manuscript entitled “Solubility of Some Drugs in Aqueous Solution of Choline Chloride-Based Deep Eutectic Solvent (DES) System: Experimental Data, Modeling and the Effect of Solution pH” has not enough novelty for publication in IJPR. The experimental section (solubility measurement) is too limited and the QSPR model is weak for publication. Choline Chloride-Based solvent as a Deep Eutectic Solvent (DES) System was used in previous research. I recommended this article refer to Journal related to computational methods.
DESs such as choline chloride-glycerol/urea recently have been used for the solubilization of drugs. Reported data (studied drugs) have been presented for the first time and the solubilization mechanism of DESs and quantitative structure property (solubilization) relationship models have been proposed. In addition, the effect of solution pH containing DES has been discussed. This issue was incorrectly ignored in the previously published articles.

Reviewer 2: The manuscript entitled “Solubility of Some Drugs in Aqueous Solution of Choline Chloride Based Deep Eutectic Solvent (DES) System: Experimental Data, Modeling and the Effect of Solution pH” is focused on the solubility studies of poorly water-soluble drugs in aqueous solutions of DES. The topic of the article is within the scope of the journal, but there are some issues that should be addressed.
1. There are several studies regarding the advantages of DESs as alternative solvents for poorly-soluble compounds. Solubility enhancement of various APIs in choline chloride-urea and choline chloride-glycerol has also been

reported in the literature. Therefore, it is suggested to clarify the novelty and significance of the study in the “Introduction”.
-DESs such as choline chloride-glycerol/urea recently have been used for the solubilization of drugs. Reported data (studied drugs) have been presented for the first time and the solubilization mechanism of DESs and quantitative structure property (solubilization) relationship models have been proposed. In addition, the effect of solution pH containing DES has been discussed. This issue was incorrectly ignored in the previously published articles.

2. Due to the instability of this type of DES in the presence of water, how appropriate was their use in this study?
-Instability of DESs (dissociation to their components) is possible in an aqueous solution. However, their components could have a significant effect on the solubility of drugs.

3. Why the solubility measurements were carried out at 37°C rather than at the room temperature?
-Body temperature was selected for the evaluation of drug solubility in the presence of DESs. As you know, the solubility of drugs is one of the main factors which affect on dissolution rate and oral bioavailability of drugs.

4. Comparing the solubility of the APIs in DESs with their solubility in a conventional pharmaceutical solvent is suggested.
-Solubility of studied drugs have been not reported in cosolvent + water mixture systematically. In addition, toxicity of conventional pharmaceutical solvent is high in compared with DES which considered as green solvent with low toxicity.

5. More details are required for the experimental section.
-We added more details to the experimental section.

6. Table 2: Footnote should be corrected (a, b, …)
-Corrected.

7. The conclusion should be improved considering the outcome of the research.
-Conclusion was revised.

8. In general, the writing needs to be improved.
-We checked the manuscript to correct English writing errors.

EIC Decision:
The novelty and significance of the study should be clarified.
-DESs such as choline chloride-glycerol/urea recently have been used for the solubilization of drugs. Reported data (studied drugs) have been presented for the first time and the solubilization mechanism of DESs and quantitative structure property (solubilization) relationship models have been proposed. In addition, the effect of solution pH containing DES has been discussed. This issue was incorrectly ignored in the previously published articles.

2 Revision 1

2 comments · 25 May 2023 – 25 May 2023

Associate Editor

ACCEPT 25 May 2023

Dear EIC,

The paper is correctly revised and presented. Therefore, publication is recommended.
Regards,

Editor-in-Chief

ACCEPT 25 May 2023

Dear Author,

I am pleased to inform you that your manuscript has been accepted for publication in Iranian Journal of Pharmaceutical Research.
Regards,