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The hydroperoxyl radical scavenging activity of sulfuretin: insights from theory

Nguyen Thi Hoa, Do Thi Ngoc Hang, Do Phu Hieu, Huynh Van Truong, Loc Phuoc Hoang, Adam Mechler and Quan V. Vo

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Review timeline

Original submission:	22 April 2021
Revised submission:	28 May 2021
Final acceptance:	10 June 2021

Note: Reports are unedited and appear as submitted by the referee. The review history appears in chronological order.

Review History

RSOS-210626.R0 (Original submission)

Review form: Reviewer 1 (Anoop Ayyappan)

Is the manuscript scientifically sound in its present form?
No

Are the interpretations and conclusions justified by the results?
No

Is the language acceptable?
Yes

Do you have any ethical concerns with this paper?
No

Have you any concerns about statistical analyses in this paper?
No

Recommendation?
Major revision is needed (please make suggestions in comments)

Comments to the Author(s)
Page 2: ONOO- or ONOO•.?
Page 3 Introduction paragraph 2. Provide the citation for Jung and coworkers ... Change inbibition to inhibition
Page 4 line 11 and Page5-line2: Change Gibb free energy to Gibbs free energy
Page 6 Table 3 caption: kECK, change k_{ECK} (subscript), and change -1 to superscript in $M^{-1}S^{-1}$
Page 6 kinetic study paragraph 2 below the table: Provide $\Delta G^{\ddagger}$ value after O3-H bond, similar to O4'-H bond above.
Page 9: The next table should be Table 4. Add a space after kcal/mol). Also change to 'As shown in Table 4'.
Page 5: The positive value 1.1 of ΔG^0 of a reaction (Table2 ΔG^0 RAF value for C2 is 1.1) does not rule out the possibility of the reaction especially considering the accuracy of the DFT calculation. The kinetics of the reaction mainly depend on the activation barrier. This is further supported by the kinetic study in this article that RAF at C8 does not contribute to the rate despite ΔG^0 being -4.6 kcal/mol. Therefore, I don't find any reason to exclude that path based only on the ΔG^0 values. To check the consistency, the calculations have to be carried out with few other methods (other functionals or wave-function based methods). The RAF path at C2 also should be included in the kinetic study.
According to PA value authors determined that the O4'-H bond is likely to dissociate. But in Figure 3 they showed the dissociation of the O6-H bond.

Review form: Reviewer 2

Is the manuscript scientifically sound in its present form?
Yes

Are the interpretations and conclusions justified by the results?
Yes

Is the language acceptable?
Yes

Do you have any ethical concerns with this paper?
No

Have you any concerns about statistical analyses in this paper?
No

Recommendation?
Accept with minor revision (please list in comments)

Comments to the Author(s)
In this manuscript, the authors report a theoretical investigation on the scavenging activity of sulfuretin natural compounds against the OOH radical. Both thermodynamic and kinetic aspects have been considered. The study has been performed considering different reaction mechanism and environments (gas-phase, lipid and aqueous). The used computational protocol is quite standard and previously used by different authors. The pKa of the compounds has been also determined.

The manuscript is of interest for the journal readers, data are well discussed and conclusions are consistent with the obtained data. The manuscript can be published after the consideration of the following minor points:
-in water phase the major part of the OOH radical is present in the dissociated form. Why the authors neglect this data;
- The captions of some tables must be implemented (i.e. in table 3 it is not clear the environment);
-The language need moderate revision;
-Some typos must be removed.

Decision letter (RSOS-210626.R0)

We hope you are keeping well at this difficult and unusual time. We continue to value your support of the journal in these challenging circumstances. If Royal Society Open Science can assist you at all, please don't hesitate to let us know at the email address below.

Dear Dr Vo:

Title: The Hydroperoxyl Radical Scavenging Activity of Sulfuretin: Insights from Theory
Manuscript ID: RSOS-210626

Thank you for your submission to Royal Society Open Science. The chemistry content of Royal Society Open Science is published in collaboration with the Royal Society of Chemistry.

The editor assigned to your manuscript has now received comments from reviewers. We would like you to revise your paper in accordance with the referee and Subject Editor suggestions which can be found below (not including confidential reports to the Editor). Please note this decision does not guarantee eventual acceptance.

Please submit your revised paper before 18-Jun-2021. Please note that the revision deadline will expire at 00.00am on this date. If we do not hear from you within this time then it will be assumed that the paper has been withdrawn. In exceptional circumstances, extensions may be possible if agreed with the Editorial Office in advance. We do not allow multiple rounds of revision so we urge you to make every effort to fully address all of the comments at this stage. If deemed necessary by the Editors, your manuscript will be sent back to one or more of the original reviewers for assessment. If the original reviewers are not available we may invite new reviewers.

To revise your manuscript, log into http://mc.manuscriptcentral.com/rsos and enter your Author Centre, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision." Your manuscript number has been appended to denote a revision. Revise your manuscript and upload a new version through your Author Centre.

When submitting your revised manuscript, you must respond to the comments made by the referees and upload a file "Response to Referees" in "Section 6 - File Upload". Please use this to document how you have responded to the comments, and the adjustments you have made. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response.

Once again, thank you for submitting your manuscript to Royal Society Open Science and I look forward to receiving your revision. If you have any questions at all, please do not hesitate to get in touch.

Yours sincerely,
Dr Laura Smith
Publishing Editor, Journals

Royal Society of Chemistry
Thomas Graham House
Science Park, Milton Road
Cambridge, CB4 0WF
Royal Society Open Science - Chemistry Editorial Office

On behalf of the Subject Editor Professor Anthony Stace and the Associate Editor Dr Debashree Ghosh.

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RSC Associate Editor:
Comments to the Author:
The authors should revise their manuscript to incorporate the comments/ suggested changes by the referees and provide a point-by-point reply to the comments before the manuscript can be accepted.

RSC Subject Editor:
Comments to the Author:
(There are no comments.)

****

Reviewers' Comments to Author:
Reviewer: 1

Comments to the Author(s)
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Reviewer: 2

Comments to the Author(s)
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-The language need moderate revision;
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Author's Response to Decision Letter for (RSOS-210626.R0)

See Appendix A.

Decision letter (RSOS-210626.R1)

We hope you are keeping well at this difficult and unusual time. We continue to value your support of the journal in these challenging circumstances. If Royal Society Open Science can assist you at all, please don't hesitate to let us know at the email address below.

Dear Dr Vo:

Title: The Hydroperoxyl Radical Scavenging Activity of Sulfuretin: Insights from Theory
Manuscript ID: RSOS-210626.R1

It is a pleasure to accept your manuscript in its current form for publication in Royal Society Open Science. The chemistry content of Royal Society Open Science is published in collaboration with the Royal Society of Chemistry.

The comments of the reviewer(s) who reviewed your manuscript are included at the end of this email.

Please see the Royal Society Publishing guidance on how you may share your accepted author manuscript at https://royalsociety.org/journals/ethics-policies/media-embargo/. After publication, some additional ways to effectively promote your article can also be found here https://royalsociety.org/blog/2020/07/promoting-your-latest-paper-and-tracking-your-results/.

Thank you for your fine contribution. On behalf of the Editors of Royal Society Open Science and the Royal Society of Chemistry, I look forward to your continued contributions to the Journal.

Yours sincerely,
Dr Laura Smith
Publishing Editor, Journals

Royal Society of Chemistry
Thomas Graham House
Science Park, Milton Road
Cambridge, CB4 0WF
Royal Society Open Science - Chemistry Editorial Office

On behalf of the Subject Editor Professor Anthony Stace and the Associate Editor Dr Debashree Ghosh.

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RSC Associate Editor
Comments to the Author:
The authors have addressed all the issues raised by the referees and I am happy to recommend that the manuscript be accepted.

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Reviewer(s)' Comments to Author:

Appendix A

Dr Laura Smith
Publishing Editor, Journals

Royal Society of Chemistry
Thomas Graham House
Science Park, Milton Road
Cambridge, CB4 0WF

Dear Prof. Smith,

We have revised our manuscript meticulously following the reviewers' recommendations. Their comments allowed us to make several improvements to the manuscript. Please see the details in the response to reviewers file. Our responses are in blue and the changes are highlighted in red in the manuscript.
We believe that the manuscript is now ready for publishing.
Thank you for your time and consideration.

Sincerely yours,

Quan Van Vo
The University of Danang - University of Technology and Education,
Danang 550000, Vietnam
Email: vvquan@ute.udn.vn
Danang, May 28, 2021

Reviewers' Comments to Author:
Reviewer: 1

Comments to the Author(s)

Page 2: ONOO- or ONOO•.?

Author reply: It is ONOO- , formed by the reaction of $O2^{\bullet-}$ with NO free radical.

Page 3 Introduction paragraph 2. Provide the citation for Jung and coworkers ... Change inbibition to inhibition

Author reply: The reference has been updated. The typo has been corrected.

Page 4 line 11 and Page5-line2: Change Gibb free energy to Gibbs free energy

Author reply: The typo has been corrected.

Page 6 Table 3 caption: kECK, change k_{ECK} (subscript), and change -1 to superscript in $M^{-1}S^{-1}$

Author reply: The typos have been corrected.

Page 6 kinetic study paragraph 2 below the table: Provide $\Delta G^{\ddagger}$ value after O3-H bond, similar to O4'-H bond above.

Author reply: The $\Delta G^{\ddagger}$ value has been added.
Page 9: The next table should be Table 4. Add a space after kcal/mol). Also change to 'As shown in Table 4'.

Author reply: Done.

Page 5: The positive value 1.1 of ΔG^0 of a reaction (Table2 ΔG^0 RAF value for C2 is 1.1) does not rule out the possibility of the reaction especially considering the accuracy of the DFT calculation. The kinetics of the reaction mainly depend on the activation barrier. This is further supported by the kinetic study in this article that RAF at C8 does not contribute to the rate despite ΔG^0 being -4.6 kcal/mol. Therefore, I don't find any reason to exclude that path based only on the ΔG^0 values. To check the consistency, the calculations have to be carried out with few other methods (other functionals or wave-function based methods). The RAF path at C2 also should be included in the kinetic study.

Author reply: The kinetic section has been updated with data for the C2 position following the RAF mechanism. However, the contribution of this reaction in the $k_{overall}$ is minor.

We acknowledge the importance of choosing the right functional for calculating kinetics; however, this was luckily studied by several groups before us, and thus we could rely on their results. The Minnesota 06 functional is among the best methods to compute both thermodynamic and kinetic parameters with good accuracy that stand the comparison with results yielded by more complex functionals (i.e. G3(MP2)-RAD) or experimental data.[1-5] The M06-2X/6-311++G(d,p) level of theory has been widely used to evaluate the radical scavenging activity of organic compounds.[1,6-11] The results obtained for RAF reactions here are also in good agreement with previous data in phenolic compounds.[9,12,13] Thus, we are confident that the data is correct and reliable at the current state of the art of computational chemistry.

According to PA value authors determined that the O4'-H bond is likely to dissociate. But in Figure 3 they showed the dissociation of the O6-H bond.

Author reply: That was an error, it has been corrected.

Reviewer: 2

Comments to the Author(s)
In this manuscript, the authors report a theoretical investigation on the scavenging activity of sulfuretin natural compounds against the OOH radical. Both thermodynamic and kinetic aspects have been considered. The study has been performed considering different reaction mechanism and environments (gas-phase, lipid and aqueous). The used computational protocol is quite standard and previously used by different authors. The pKa of the compounds has been also determined.
The manuscript is of interest for the journal readers, data are well discussed and

conclusions are consistent with the obtained data. The manuscript can be published after the consideration of the following minor points:

-in water phase the major part of the OOH radical is present in the dissociated form. Why the authors neglect this data;

Author reply: We thank the reviewer for this suggestion. The $HOO^{\bullet}$ could be deprotonated to form $O_2^{\bullet-}$ in water. Thus this process could be included in the rate constant by considering the molar fraction (f) of $HOO^{\bullet}$ (at pH = 7.40, f($HOO^{\bullet}$) = 0.0025). However, if we perform this adjustment for the reference antioxidants as well as the studied compounds, the values of rate constant will change to a similar degree; thus the trend is not affected only the absolute value. Therefore we did not include the deprotonation of $HOO^{\bullet}$. Since $O_2^{\bullet-}$ radical does not present in lipid media i.e., pentyl ethanoate, thus $HOO^{\bullet}$ has been used as a model radical to evaluate the radical scavenging activity of antioxidants in the physiological environment.[9,14-17]

- The captions of some tables must be implemented (i.e. in table 3 it is not clear the environment);

Author reply: The necessary information has been updated.

-The language need moderate revision;
-Some typos must be removed.

Author reply: The manuscript has been carefully revised, all of typos have been corrected.

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