

1. PROSES SUBMIT



wiwied ekasari <wiwied-e@ff.unair.ac.id>

Manuscript submitted to Veterinary Medicine International

5 messages

Veterinary Medicine International <sarah.viscarra@hindawi.com>
To: wiwied-e@ff.unair.ac.id

Sun, Nov 21, 2021 at 8:43 PM



Dear Dr. Ekasari,

Congratulations, the manuscript titled "Toxicological Evaluation and Protective Effects of Ethanolic Leaf Extract of Cassia spectabilis on Liver and Kidney Function of Plasmodium berghei-Infected Mice" has been **successfully submitted** to Veterinary Medicine International.

We will confirm this submission with all authors of the manuscript, but you will be the primary recipient of communications from the journal. As submitting author, you will be responsible for responding to editorial queries and making updates to the manuscript.

In order to view the status of the manuscript, please visit the manuscript details page.

Thank you for submitting your work to Veterinary Medicine International.

[MANUSCRIPT DETAILS](#)

Kind regards,
Sarah Viscarra
Veterinary Medicine International

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Veterinary Medicine International <sarah.viscarra@hindawi.com>
To: wiwied-e@ff.unair.ac.id

Mon, Nov 22, 2021 at 8:40 AM

[Quoted text hidden]

wiwied ekasari <wiwied-e@ff.unair.ac.id>
To: Veterinary Medicine International <sarah.viscarra@hindawi.com>

Mon, Dec 6, 2021 at 11:53 AM

Dear
Miss Sarah Viscarra
Veterinary Medicine International

I want to ask you about my manuscript ID 6770828 (title : Toxicological Evaluation and Protective Effects of Ethanolic Leaf Extract of Cassia spectabilis on Liver and Kidney Function of Plasmodium berghei-Infected Mice)

As requested, all co-authors have already created Hindawi accounts.

But until now, the detailed manuscript information states that my manuscript is in a position of pending approval. Are there any other requirements that I need to complete, because I didn't find this information.

Thank you very much, I'm waiting to hear from you

Best regards,
Dr. Wiwied Ekasari, MSi., Apt

[Quoted text hidden]

Sarah Vizcarra <sarah.viscarra@hindawi.com>
Reply-To: Sarah Vizcarra <sarah.viscarra@hindawi.com>
To: wiwied-e@ff.unair.ac.id

Mon, Dec 6, 2021 at 4:49 PM

Dear Dr. Ekasari,

Thank you for your inquiry. The Editor who is overseeing the review process of your manuscript is currently assigning it to external reviewers. Once the reviewers have submitted their reports, the Editor will be able to make a decision.

We will notify you when the decision is finalized.

Best regards,

Sarah

Sarah Viscarra
Editorial Assistant



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[Quoted text hidden]

wiwied ekasari <wiwied-e@ff.unair.ac.id>
To: Sarah Vizcarra <sarah.viscarra@hindawi.com>

Mon, Dec 6, 2021 at 8:33 PM

Dear
Miss Sarah Viscarra
Veterinary Medicine International

Thank you very much for the information. Hope to get good news from you soon.

Best regards,

Dr. Wiwied Ekasari
[Quoted text hidden]

2. PROSES REVIEW



wiwied ekasari <wiwied-e@ff.unair.ac.id>

6770828: Revision requested

4 messages

Hikasa Yoshiaki <support@hindawi.com>
Reply-To: Sarah Sarah <sarah.viscarra@hindawi.com>
To: Ekasari Wiwied <wiwied-e@ff.unair.ac.id>

Thu, Dec 9, 2021 at 4:14 PM



Dear Ekasari Wiwied,

In order for your submission "Toxicological Evaluation and Protective Effects of Ethanolic Leaf Extract of *Cassia spectabilis* on Liver and Kidney Function of *Plasmodium berghei*-Infected Mice" to Veterinary Medicine International to proceed to the review process, there **needs to be a revision**.

Reason & Details:

“

This manuscript involves the interesting findings about the toxic and protective effects of ethanol extract of *Cassia spectabilis* leaves on the liver and kidneys of mice infected with *Plasmodium berghei* ANKA. However, the reviewer required a minor revision of this manuscript. Please carefully read the reviewer report, and correct, mention and/or reply for all of the specific points suggested by the reviewer. The editor looks forward to the submission of the revised manuscript.

For more information about what is required, please click the link below.

MANUSCRIPT DETAILS

Kind regards,
Hikasa Yoshiaki

Veterinary Medicine International

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Updated on 2021-11-21

Version 1

Toxicological Evaluation and Protective Effects of Ethanolic Leaf Extract of *Cassia spectabilis* on Liver and Kidney Function of *Plasmodium berghei*-Infected Mice

[VIEWING AN OLDER VERSION](#)

ID 6770828

Wiwied Ekasari ^{SA CA} ¹, Anisah Mahardiani¹,
Nindya Tresiana Putri¹, Tutik Sri Wahyuni¹, Heny Arwati²

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Article Type

Research Article

Journal

Veterinary Medicine
International

Academic Editor Hikasa Yoshiaki

Submitted on 2021-11-21 (2 months ago)

> [Abstract](#)

> [Author Declaration](#)

> [Files](#) 2

– Editorial Comments

Recommendation

Yoshiaki Hikasa AE 09.12.2021

Minor Revision Requested

Message for Author

This manuscript involves the interesting findings about the toxic and protective effects of ethanol extract of *Cassia spectabilis* leaves on the liver and kidneys of mice infected with *Plasmodium berghei* ANKA. However, the reviewer required a minor revision of this manuscript.

Please carefully read the reviewer report, and correct, mention and/or reply for all of the specific points suggested by the reviewer. The editor looks forward to

All our journals remain open as normal during the COVID-19 crisis. However, if you are unable to carry on with your activities as normal, please contact help@hindawi.com and we will work with you to find a solution.

> **Abstract**

> **Author Declaration**

> **Files** 2

– Editorial Comments

Recommendation

Yoshiaki Hikasa AE 09.12.2021

Minor Revision Requested

Message for Author

This manuscript involves the interesting findings about the toxic and protective effects of ethanol extract of *Cassia spectabilis* leaves on the liver and kidneys of mice infected with *Plasmodium berghei* ANKA. However, the reviewer required a minor revision of this manuscript.

Please carefully read the reviewer report, and correct, mention and/or reply for all of the specific points suggested by the reviewer. The editor looks forward to the submission of the revised manuscript.

– Reviewer Reports

1 submitted

Report

Reviewer 1 04.12.2021

- Introduction : The criteria or rational for using this plant should be added more, and if this extract has previously been studied, it should be added more as well.
- Toxicity assay : According yo OECD guideline, the tested compound should not administer > 5,000 mg/kg, the authors used > 5,000 mg/kg in acute toxicity, please clarify.
- Enzyme assay : Liver damage was determined using SGOT and SGPT activities, how about kidney injury indicators? BUN and creatinine are mostly used as indicators, why do not the author use these markers for indicating kidney injury?
- Discussion : This plant extract has been done before about antimalarial activities in both in vitro and in vivo studies, the authors should add more comparison or discussion between suppressive assay from this study with the previous ones. Moreover, the possibility mechanisms or active compounds in the extract should also be discussed. As this plant extract exerted antimalarial activity in good character, the author should discuss more about the protective effect in liver and kidney during malaria infection whether come from antimalarial activity or the direct effect of the extract or not.

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wiwied ekasari <wiwied-e@ff.unair.ac.id>
To: Sarah Sarah <sarah.viscarra@hindawi.com>

Thu, Dec 9, 2021 at 9:05 PM

Dear
Mr. Hikasa Yoshiaki

Thank you very much for your email.
Yes, I will revise the manuscript according to the reviewer's suggestion.

Best regards,
Dr. Wiwied Ekasari, MSi., Apt
[Quoted text hidden]

wiwied ekasari <wiwied-e@ff.unair.ac.id>
To: Sarah Sarah <sarah.viscarra@hindawi.com>

Sat, **Jan 1, 2022** at 7:01 AM

Dear Mr. Hikasa Yoshiaki
Veterinary Medicine International

I inform you that I have **submitted a revision** of my manuscript entitled "Toxicological Evaluation and Protective Effects of Ethanolic Leaf Extract of *Cassia spectabilis* DC on Liver and Kidney Function of *Plasmodium berghei*-Infected Mice" by system. Here I also send my revision file.

Best regards
Dr. Wiwied Ekasari., MSi., Apt

On Thu, Dec 9, 2021 at 4:14 PM Hikasa Yoshiaki <support@hindawi.com> wrote:
[Quoted text hidden]

2 attachments

 **Revisi-Hindawi_template_C spectabilis_final.docx**
892K

 **Answer Reviewer Comment final.docx**
21K

Sarah Vizcarra <sarah.viscarra@hindawi.com>
Reply-To: Sarah Vizcarra <sarah.viscarra@hindawi.com>
To: wiwied-e@ff.unair.ac.id

Mon, Jan 3, 2022 at 5:59 AM

Dear Dr. Ekasari,

Thank you for the information.

In this unprecedented time, Hindawi remains open and committed to publishing peer-reviewed academic work as normal. However, we realize that due to the current pandemic you may require more time to respond to us, or may even be unable to carry on with your normal academic activities. We are here to help and so if you are

either unable to carry on or need more time, please reply to this email and we will work with you to find a solution.

Best regards,

Sarah

Sarah Viscarra
Editorial Assistant



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[Quoted text hidden]

▪ Review report(s)

Recommendation

Minor Revision Requested

Yoshiaki Hikasa

AE

Message For Author

This manuscript involves the interesting findings about the toxic and protective effects of ethanol extract of *Cassia spectabilis* leaves on the liver and kidneys of mice infected with *Plasmodium berghei* ANKA. However, the reviewer required a minor revision of this manuscript. Please carefully read the reviewer report, and correct, mention and/or reply for all of the specific points suggested by the reviewer. The editor looks forward to the submission of the revised manuscript.

Reviewer 1

- (iii) Introduction : The criteria or rational for using this plant should be added more, and if this extract has previously been studied, it should be added more as well.
- (iv) Toxicity assay : According yo OECD guideline, the tested compound should not administer > 5,000 mg/kg, the authors used > 5,000 mg/kg in acute toxicity, please clarify.
- (v) Enzyme assay : Liver damage was determined using SGOT and SGPT activities, how about kidney injury indicators? BUN and creatinine are mostly used as indicators, why do not the author use these markers for indicating kidney injury?
- (vi) Discussion : This plant extract has been done before about antimalarial activities in both in vitro and in vivo studies, the authors should add more comparison or discussion between suppressive assay from this study with the previous ones. Moreover, the possibility mechanisms or active compounds in the extract should also be discussed. As this plant extract exerted antimalarial activity in good character, the author should discuss more the protective effect in liver and kidney during malaria infection whether come from antimalarial activity or the direct effect of the extract or not.

▪ Answer to reviewer(s)

1. Reviewer:

Introduction : The criteria or rational for using this plant should be added more, and if this extract has previously been studied, it should be added more as well.

ANSWER: We have added the explanation on the previous studies of the extract in lines 48– 55.

“Previous studies reported that an *in vivo* test on the 90% ethanol extract of *C. spectabilis* DC leaf against *P. berghei* ANKA in BALB/c mice showed an ED₅₀ value was 131.5 mg/kg BW [9], and categorized as very good antimalarial activity [10]. Furthermore, the extract, fractions, sub -fractions, and isolated compound of *C. spectabilis* DC have been tested *in vitro* for their antimalarial activities. The active compound of this plant has been successfully identified as a compound that identical to (–)-7-hydroxycassine, and its *in vitro* antimalarial activity test showed a very low IC₅₀ of 0.016 µg/mL [11], that classified as a very strong antimalarial activity [12].”

2. Reviewer:

Toxicity assay : According to OECD guideline, the tested compound should not administer > 5,000 mg/kg, the authors used > 5,000 mg/kg in acute toxicity, please clarify.

ANSWER: Yes, because of this guideline, therefore we removed the concentration more than 5,000 mg/kg BW (lines 116–117). We then revised the method, results and discussion regarding this removal (lines 116–117; 164–171; and 252–255). The reason is that there is no mouse died at the highest concentration of the extract (5,000 mg/kg BW) suggested that the extract is not toxic to the mice.

3. Reviewer:

Enzyme assay : Liver damage was determined using SGOT and SGPT activities, how about kidney injury indicators? BUN and creatinine are mostly used as indicators, why do not the author use these markers for indicating kidney injury?

ANSWER:

- The enlargement of the liver (hepatomegaly) usually occurs in malaria infection, but there is no enlargement of the kidney, therefore, we are more focused on the histopathology as well as the biochemistry of the liver. The histopathology of the kidney is more important to find out the damaged cells due to malaria infection and or extract administration. The explanation above has been added to the lines 65–77.
- Evaluation of the effect of EECS was determined both through histopathology and biochemistry examinations. We considered that the biochemistry data will give further confirmation for any liver and kidney failure. However, we more concentrated on the liver, because there is enlargement of liver (hepatomegaly) in malaria infection, but there is no enlargement in the kidney. Therefore, the data of BUN and creatinine is not the major data needed in this study. The data on histopathology of the kidney is more important to find out the damage of the tissue whether do toe malaria infection or the administration of the extract. The explanation regarding this data has been added to the manuscript (lines 210– 214).

4. Reviewer:

Discussion : This plant extract has been done before about antimalarial activities in both in vitro and in vivo studies, the authors should add more comparison or discussion between suppressive assay from this study with the previous ones. Moreover, the possibility mechanisms or active compounds in the extract should also be discussed. As this plant extract exerted antimalarial activity in good character, the author should discuss more the protective effect in liver and kidney during malaria infection whether come from antimalarial activity or the direct effect of the extract or not.

ANSWER:

- The suppressive test in this study was done to obtain the blood of extract-treated infected mice prior to biochemistry examination. The method is as same as we have done in the previous study [Ekasari et al., 2021]. Therefore, as not to impress duplicating the research, we have revised the title of this section to: The effect EECS to the serum level of SGOT and SGPT (line 131).
- The possible mechanism of the active compound has not been done. Only the extract has been tested in heme detoxification [Ekasari et al., 2021]. We have added this explanation in lines 298–301.
- The discussion on the protective effect of the extract to the liver and kidney has been added to the lines 267–279 and 292–297.

3. ARTIKEL DITERIMA UNTUK PUBLIKASI



wiwied ekasari <wiwied-e@ff.unair.ac.id>

Your manuscript has been accepted for publication

1 message

Veterinary Medicine International <sarah.viscarra@hindawi.com>
To: wiwied-e@ff.unair.ac.id

Thu, Jan 13, 2022 at 7:30 PM



Dear Dr. Ekasari,

I am delighted to inform you that the review of your Research Article 6770828 titled Toxicological Evaluation and Protective Effects of Ethanolic Leaf Extract of *Cassia spectabilis* DC on Liver and Kidney Function of Plasmodium berghei-Infected Mice has been completed and your **article has been accepted for publication** in Veterinary Medicine International.

Please visit the manuscript details page to review the editorial notes and any comments from external reviewers. If you have deposited your manuscript on a preprint server, now would be a good time to update it with the accepted version. If you have not deposited your manuscript on a preprint server, you are free to do so.

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Files requested - Toxicological Evaluation and Protective Effects of Ethanolic Leaf Extract of *Cassia spectabilis* DC on Liver and Kidney Function of *Plasmodium berghei*-Infected Mice

1 message

Quality Checking Team <support@hindawi.com>
To: wiwied-e@ff.unair.ac.id

Thu, Jan 13, 2022 at 7:33 PM



Dear Dr. Wiwied Ekasari,

Regarding your manuscript Toxicological Evaluation and Protective Effects of Ethanolic Leaf Extract of *Cassia spectabilis* DC on Liver and Kidney Function of *Plasmodium berghei*-Infected Mice 6770828, we would be grateful if you could please address the following:

- Please **upload editable figure files and tables separately**.
 - Please upload the editable versions (with High resolution) of the figures in a single ZIP file under the Figures & Tables section. None of the figures can be edited. We need to be able to edit lines arrowheads and fonts to match the journal's style. Each figure should be a separate ps eps ai Visio wmf emf Word Excel PowerPoint or PDF file which can be edited. Please note that jpg bmp png and tiff files cannot be edited by default.

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5. When all necessary changes have been made, click the green "Submit manuscript" button at the bottom of the screen, and this will return the manuscript to the Hindawi team.

Kind regards,
Quality Checking Team

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4. ARTIKEL DITERBITKAN



wiwied ekasari <wiwied-e@ff.unair.ac.id>

6770828: Your article has been published

2 messages

Sarah Viscarra <sarah.viscarra@hindawi.com>
To: wiwied-e@ff.unair.ac.id

Wed, Feb 16, 2022 at 11:16 AM

Dear Dr. Ekasari,

I am pleased to let you know that your **article has been published** in its final form in "Veterinary Medicine International."

Wiwied Ekasari, "Toxicological Evaluation and Protective Effects of Ethanolic Leaf Extract of Cassia spectabilis DC on Liver and Kidney Function of Plasmodium berghei-Infected Mice," Veterinary Medicine International, vol. 2022, Article ID 6770828, 9 pages, 2022. <https://doi.org/10.1155/2022/6770828>.

You can access this article from the Table of Contents of Volume 2022, which is located at the following link:

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If you would like to order reprints of this article please click here, <https://www.hindawi.com/journals/vmi/2022/6770828/reprint/>.

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Thank you for publishing your article with Hindawi, and we hope that you continue to choose Veterinary Medicine International as a home for your research.

Best regards,

Sarah Viscarra
Veterinary Medicine International
Hindawi
<https://www.hindawi.com/>

wiwied ekasari <wiwied-e@ff.unair.ac.id>
To: Sarah Viscarra <sarah.viscarra@hindawi.com>

Wed, Feb 16, 2022 at 11:48 AM

Dear Sarah Viscarra
Veterinary Medicine International
Hindawi

Thank you very much for your email.
I am very happy to hear this news. I hope we can collaborate next time

Best Regard,
Dr. Wiwied Ekasari., MSi Apt