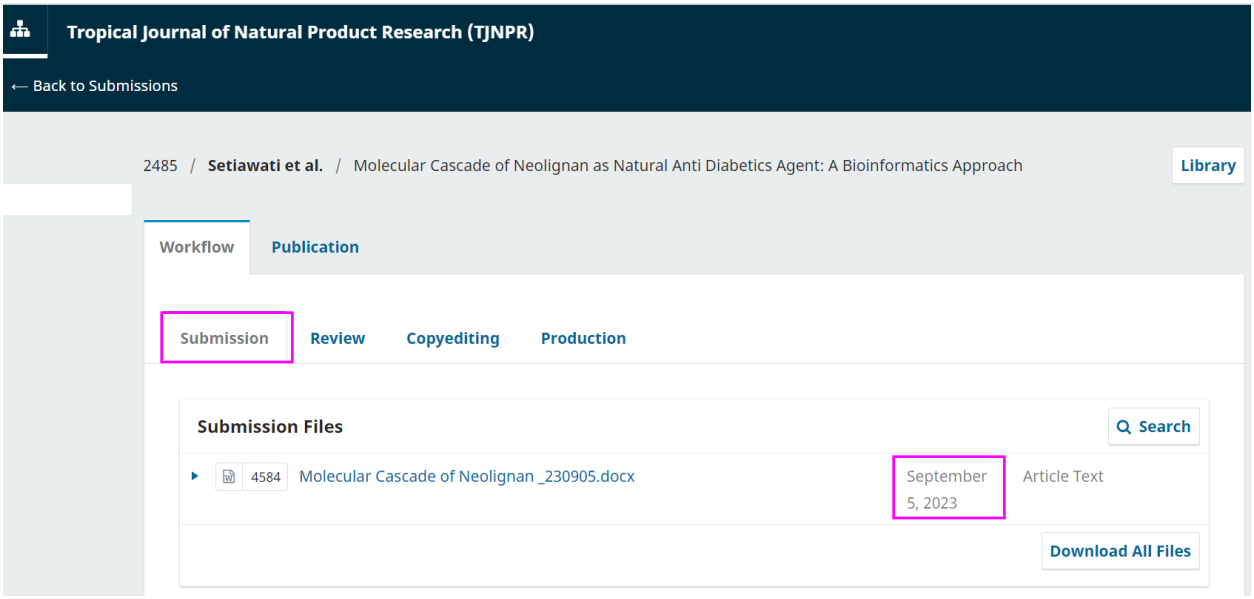
No	Tahap Korespondensi Publikasi “Molecular Cascade of Neolignan as Natural Anti Diabetics Agent: A Bioinformatics Approach"	Tanggal
1.	Manuscript submission	4 September 2023
2.	Rekomendasi reviewer list	4 September 2023
3	Manuscript decision: Revision needed from two referees	10 Oktober 2023
4.	Revisi manuskrip	13 Oktober 2023
5.	Manuscript decision: Provisional Acceptance Letter	27 Oktober 2023
6.	English Proofread certificate	13 November 2023
7	Galley Proofread	17 November 2023
8	Online manuscript published	1 Desember 2023

1. Manuscript submission



2. Reviewer Rekomendasi List

{TJNPR} Manuscript Submission Request

Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>

To:Agustina Setiawati <nina@usd.ac.id>

Thank you for submitting your original manuscript to the Tropical Journal of Natural Product Research (TJNPR) www.tjnpr.org

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(https://www.scopus.com/sourceid/21100933230).

kindly suggest four (4) competent reviewers { two (2) foreign/international, two (2) National/from your country}. Their names, university-based email addresses and affiliations should be submitted.

The email addresses of all the authors should also be submitted

The peer-review process will commence immediately, as the manuscript will be passed to an editor for initial assessment as soon as possible. If there are any problems with your submission, we will contact you. Also, note that manuscripts submitted and undergoing peer review will not be accepted for withdrawal or retraction.

Title: **Molecular Cascade of Neolignan as Natural Anti Diabetics Agent: A Bioinformatics Approach**

Best regards

Abiodun

Professor Abiodun Falodun, PhD: FAAS, FISPON

Editor-in-Chief:
Tropical Journal of Natural Product Research (TJNPR)
Head, Natural Product Research Group, University of Benin
Email: editor.tjnpr@gmail.com
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Re: {TJNPR} Manuscript Submission Request

Agustina Setiawati <nina@usd.ac.id>

To:Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>

Dear Editor,

Herewith I am sending, the list of our suggested reviewers:

1. Rifki Febriansah

Muhammadiyah University of Yogyakarta
rifki.febriansah@umy.ac.id

2. Adam Hermawan

Faculty of Pharmacy, Universitas Gadjah Mada
adam_apt@ugm.ac.id

3. L. Hartanto Nugroho

Faculty of Biology, Universitas Gadjah Mada
hartantonugroho2005@ugm.ac.id

4. Jia Chen & Jianhua Shao,

Jiangsu Key Laboratory of Crop Genetics
Physiology/Co-Innovation Center for Modern Production Technology of Grain Crops,
Yangzhou University, Yangzhou 225009, P.R. China,
chartishchen@hotmail.com
jhshao@yzu.edu.cn

5. Ya Li

State Key Laboratory of Applied Organic Chemistry,
College of Chemistry and Chemical Engineering,
Lanzhou University, Lanzhou 730000, China

I am looking forward to hearing from you.

Sincerely,
Agustina

3. Manuscript decision: Revision needed from two referees.

[Revised Manuscript TJNPR-2023-M474]

ET

Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>
To: Agustina Setiawati

Tue 10/10/2023 12:00 AM

badRevised_Molecular Casca...
2 MB

A manuscript not complying with these and other instructions will not be processed and may be rejected.

Submit the following files after a thorough and comprehensive revision of the manuscript

1. The revised and edited manuscript
2. The list of responses to reviewers' comments
3. Evidence of plagiarism check (**17% allowed**)
4. Evidence of grammar check

Best regards

Abiodun

Professor Abiodun Falodun, PhD; FAAS, FISPON

4. First revision of the manuscript

[Revised Manuscript TJNPR-2023-M474]

Agustina Setiawati
To: Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>
Cc: Yustina Sri Hartini; Dewi Setyaningsih

Fri 10/13/2023 10:44 AM

Revised_Molecular_Cascade_... 2 MB | TJNPR-Language certificate.p... 236 KB | Comments to Reviewers.docx 27 KB | Turnitin Neolignan as A Natu... 4 MB

4 attachments (6 MB) Save all to OneDrive - Universitas Sanata Dharma Download all

Dear Prof. Prof Abidoun,

We hereby resubmit our manuscript "*Molecular Cascade of Neolignan as A Natural Anti-Diabetics Agent: A Bioinformatics Approach*" that you handled as the responsible editor in a prior submission.

We were delighted to see that the referees expressed an interest in the work. We have taken their comments seriously and have responded to all recommendations, as detailed below. We appreciate your response to our original submission and the comments of the reviewers. We hope that the revisions made to the manuscript raise it to the high standard expected of submissions Tropical Journal of Natural Product Sciences. Moreover, we added one author in the manuscript who helps during manuscript revision.

I will continue to serve as the corresponding author for this manuscript. Please do not hesitate to contact me if you have further questions or concerns.
Please find in the attachment our revised manuscript along with the response to the reviewers, similarity check result (16%) and language certificate.

Thank you, I am looking forward to hearing from you.

Best regard,
Agustina

Reviewer #1

Section	Reviewer Comments	Responses
Title	Research title is mostly appropriate	Thank you for your positive feedback.
Abstract	The abstract word count < 250. Grammatical, spelling and punctuation errors should be corrected. • The abstract captured the entirety of the manuscript	We thank for your positive comment. We revised our manuscript accordingly grammatical, spelling, and punctuation errors.
Keywords	The keywords are based on the journal guideline	Thank you for your reminder. We followed the journal guideline for the keyword
Introduction	The aim and objectives of the research should be emphatic and made obvious. The research novelty was lacking.	We thank to the reviewer for suggestions which elevate the quality of our manuscript.
	• The authors should discuss the relevance of the adopted methods to the research.	Thank you for very positive feedback. We added the adopted method for molecular docking and bioinformatics in introduction and discussion part.
	• The relevance of Natural antidiabetic remedies should be reemphasized.	We inserted more natural remedies for antidiabetics in the third paragraph as following sentence. *"Different medicinal plants or plant extracts that include chemical components such as flavonoids, alkaloids, phenolic compounds, terpenoids, saponins, and phytosterols have shown effectiveness in treating complications associated with diabetes. This efficacy can be linked to their ability to improve chronic high blood sugar levels, reduce oxidative stress, and influence various metabolic processes that play a role in the development of diabetic complications".*
	• The STITCH and STRING protocols and their relevance to the research should be discussed briefly	We appreciate for the comment. We added a sentence to the introduction as mentioned below: "*Thus, this study utilized both STITCH and STRING to obtain the direct and indirect gen/protein interfered with by neolignan.*"

	• Recent literatures on computational-based drug discovery for diabetes should be discussed.	We thank for a very positive comment. Here, we added computational-based drug discovery for diabetes in our Introduction section. "*Furthermore, the use of protein-ligand docking, and simulation techniques has significantly applied to identify the identification of new medications for diabetes. There were previous molecular docking studies employed AutoDock 4.2 with Lamarckian Genetic Algorithm (Lamarckian GA), and Molecular Operating Environment (MOE) software to determine RMSD value, binding energy and S-score as the parameters (Tan et al., 2019) (Arief et al. (2021) (Swilam et al., 2021). A study by Arief et al. (2021) conducted molecular docking of peptides from M. charantia against SGLT1, DPP IV, and GLUT2. While other studies applied α-amylase, β-glucosidase, and pancreatic lipase (Swilam et al., 2021). This study used AutoDock 4.2 to explore neolignan ability to bind to diabetic-related protein.*"
	• The relevance of protein-protein interactions to the research should be discussed briefly – previous research validating the PPI protocol should be discussed.	Thank you for the comments. We added in our manuscript this section. "*Thus, protein-protein interaction (PPI) network was constructed to determine neighbourhood information, shortest path, distance, and modularity of interacting proteins. PPI network was validated by high-throughput experiment, including in vitro, in vivo, and in silico methods (Peng et al., 2017).*"
	• Neolignan antidiabetic properties were discussed sufficiently however, authors should include a comparative study of the Neolignans moiety and other antidiabetic-based moieties based on either computational, in vitro, in vivo or clinical trials. Citation before period	Thank you for the comments. We added in our manuscript this section. *"Neolignans linked to 2-styryl-1,3-dioxane at 8-9' containing Torreya yunnanensis inhibited in vitro phosphodiesterase 9A (PDE9A) activity which play crucial role in insulin secretion (Cheng, 2014). Thus, neolignan containing extract of the leaves of Eugenia sonderiana has shown remarkable effectiveness in both laboratory and real-life settings for decreasing blood glucose levels and enhancing diabetic conditions. This is achieved through the inhibition of amylase and glucosidase activity, as evidenced in studies involving diabetic mice. (Bastos, 2023)."*
	• The introduction is mostly sufficient however, the authors should improve on it as recommended	
Methodology	Grammatical, spelling and punctuation errors should be corrected. All syntax errors should be corrected too. The CPU and GPU specifications used should be mentioned. • The methods used for the research is mostly appropriate for the study.	We appreciate the feedback regarding the need to perform a comprehensive grammar and vocabulary review of the manuscript to correct any spelling errors. We recognize the importance of maintaining precise and high-quality language usage, and we are fully dedicated to addressing this feedback diligently.
Results	All supplementary documents associated with the research should be provided. The research results should be presented based on the journal guideline. • The results obtained is mostly appropriate for the results obtained	Thank you for a very positive comment.
Discussion	Only significant findings should be discussed explicitly. • The manuscript discussions are mostly sufficient and appropriate for the research	Thank you for your constructive comment.
Conclusion	The authors failed to capture the research future prospects	This funding provides a fundamental data to investigate *in vitro* and *in vivo* activities of neolignan as a prospective novel anti-diabetic agent.
References	The references should strictly follow the journal guideline	Thank you for your valuable input. We appreciate your recommendation to follow journal guideline and include more relevant articles in the introduction section. Therefore, we revised the references to incorporate these suggested articles and provide a more comprehensive overview of the existing research in the field.
Figures	The figures should be of the highest quality. Figure as mentioned in the manuscript shouldn't be bolded. All figures were captured and mentioned in the manuscript	Thank you for your valuable feedback. We have addressed your suggestion by revising the figures.

Tables	Tables should be numbered using Arabic numerals only. Tables as mentioned in the manuscript shouldn't be bolded. All tables were captured and mentioned in the manuscript	Thank you for your valuable feedback. We have addressed your suggestion by revising the tables.

Reviewer #2

Sections	Comments	Responses
Title	The title is mostly appropriate	Thank you for your positive feedback.
Abstract	The abstract word count is < 250. Authors should correct all grammatical and punctuation errors. • The abstract is mostly appropriate	Thank you for your positive comment.
Keywords	Keywords are mostly appropriate.	We appreciate your comment.
Introduction	Citation then period. The authors should make the aim and objectives obvious. The novelty of the research was lacking. The relevance of the methods used in the research should be discussed in brief.	Thank you for your valuable feedback. We revised our manuscript accordingly.
	The antidiabetic activities of natural product sources of neolignan should be discussed in brief. The structure of neolignan and their derivatives should be given and discussed briefly in relation to their antidiabetic activities.	Thank you for your valuable comments. Thus, we inserted the neolignane containing natural product in our introduction, as well as the structure and their derivative (along with Reviewer 1 comment) Neolignan is a large group of compounds, thus describing the derivatives may be too broad in the introduction part. Thus, we elaborate the revised manuscript along with Reviewer #1 response, as mentioned below: *"Neolignans linked to 2-styryl-1,3-dioxane at 8-9' containing Torreya yunnanensis inhibited in vitro phosphodiesterase 9A (PDE9A) activity which play*

		crucial role in insulin secretion (Cheng, 2014). Thus, neolignan containing extract of the leaves of Eugenia sonderiana has significant in vitro and in vivo in lowering glucose levels in the blood and improving diabetic conditions through amilase and glucosidase inhibition activity, including diabetic mice (Bastos, 2023).
	The various targets in the design of drugs for diabetes (MAPKs, TGF-β, VEGF, TNF-α, NF-kB) should be discussed briefly.	Thank you for your valuable comment. Here, we are adding the short discussion of MAPKs, TNF-α targeted drug for diabetes, which are also targeted by our compound; neolignan. *"Another neolignan downstream target is MAPKs, a protein kinase in glucose homeostasis, which is also targeted by metformin, a commercial anti-diabetic (Schultze et al., 2012; He et al.,2021). Moreover, neolignan targets TNF-α, a proinflammatory cytokine playing important role in developing insulin resistance if it is overexpressed in myocyte and adipocyte. Since it is targeted by metformin and piolglitazone (Saxena et al, 2020), neolignan may be a promising agent for diabetes therapy"*
	Herbal remedies rich in neolignan should be highlighted alongside their antidiabetic based medicinal values.	We added to the manuscript accordingly along with Reviewer #1 comment. "*Different medicinal plants or plant extracts that include chemical components such as flavonoids, alkaloids, phenolic compounds, terpenoids, saponins, and phytosterols have shown effectiveness in treating complications associated with diabetes. This efficacy can*

5. Manuscript decision

ET

Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>
To: Agustina Setiawati

Provisional acceptance 164.pdf
359 KB

Dear Dr Agustina Setiawati,

The manuscript submitted to the Tropical Journal of Natural Product Research www.tjnpr.org Q3 https://www.scopus.com/sourceid/21100933230 has been carefully reviewed by competent experts.

Find attached the details of the decision.

Please send your response urgently to the Editor-in-Chief, to enable us to process your manuscript for the next issue **Vol 7 issue 10, 2023.** Kindly acknowledge the receipt of the mail.
Title: Molecular Cascade of Neolignan as Natural Anti Diabetics Agent: A Bioinformatics Approach

Authors: Yustina Sri Hartini, Brigitta Amanda Maharani, Bakti Wahyu Saputra, Dewi Setyaningsih, Agustina Setiawati*

TJNPR Editorial Decision: accepts with moderate corrections

Congratulations.

TJNPR is now Q3

https://www.scimagojr.com/journalsearch.php?q=21100933230&tip=sid

Best regards

Abiodun

6. English Proofreading

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CERTIFICATE OF EDITING

This is to certify that the paper titled "**Molecular Cascade of Neolignan as A Natural Anti-Diabetics Agent: A Bioinformatics Approach**" commissioned to us by Agustina Setiawati has been edited for English language, grammar, punctuation, and spelling by Enago, the editing brand of Crimson Interactive Pvt. Ltd under Advance Editing.

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Goregaon (W), Mumbai 400062, India.
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Disclaimer: The author is free to accept or reject our changes in the document after our editing. However, we do not bear responsibility for revisions made to the document after our edit on October 13, 2023.

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7. Galley Proof before Published

Agustina Setiawati
To: Editorial Team <et.tjnpr@gmail.com>
Cc: Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>

TJNPR-2023-M474-Galley-Pr...
1 MB

Dear Editor-in-Chief,

Please find the following revision of our galley proof. We revised all the reviewer comments, including the grammar, and pages of paper we cited in our references.

Some references are not properly in place due to the Table's appearance being different from the original manuscript. Therefore, we revised it accordingly.

Thank you.

Best regards,
Agustina

...

Reply | Reply all | Forward

ET

Editorial Team <et.tjnpr@gmail.com>
To: Agustina Setiawati
Cc: Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>

TJNPR-2023-M474-Galley-Pr...
1 MB

Dear Author,
See the attached **galley proof** manuscript with title "**Molecular Cascade of Neolignan as A Natural Anti-Diabetics Agent: A Bioinformatics Approach**" for authors perusal
Please, as soon as possible (not later than 48 hours) kindly respond with receipt along with any comment or observations. Also respond to the comment(s) where indicated.

Note:
Failure to address all comments raised would cause the manuscript to be dropped from publication in this issue.

Failure to return the revised version of the galley proof (at the given time period) would cause the manuscript to be dropped from publication in this issue.

All corrections/changes made in the manuscript should be highlighted in yellow ink when submitting the manuscript in the revised form.

Best regards