Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

Bukti Korespondensi

Judul Artikel: Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves.

No	Proses	Tanggal
1	Artikel di ajukan ke jurnal *Tropical Journal of Natural Product Research*	13-9-2021
2	Artikel dalam proses review	14-9-2021
3	Revisi pertama: *accepted with moderate corrections*	27-9-2021
4	Editor mengirim hasil review artikel • Review form	21-10-2021
5	Author mengirimkan hasil revisi artikel • Response to reviewer • Plagiarism check • Revised article	26-10-2021
6	Revisi kedua: Minor revisions	10-11-2021
7	Author mengirimkan hasil revisi artikel • Response to reviewer • Plagiarism check • Revised article	15-11-2021
8	Manajer editor mengirimkan *galley proof*	2-12-2021
9	Author mengirimkan kembali kepada manajer editor hasil revisi *galley proof*	2-12-2021
10	Artikel dipublikasi pada *Tropical Journal of Natural Product Research*. Vol. 5. Issue 11. Desember 2021	5-12-2021

1. Artikel di ajukan ke jurnal *Tropical Journal of Natural Product Research*

(13-9-2021)

Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

Submited article

apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>
Mon 9/13/2021 10:13 AM
To:Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>;Managing Editor TJNPR <p.editor.tjnpr@gmail.com>
Cc:rollando2008@gmail.com <rollando2008@gmail.com>

6 attachments (482 KB)
Abstract.docx; Authors Contributor.docx; Cover latter.doc; DECLARATION AND COPYRIGHT TRANSFER FORM.docx; Manuscript_Rollando.docx; Potential Reviewer.docx;

Dear Prof. Abiodun Falodun, PhD

I am herewith submitting the manuscript entitled "Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves" for publication in Tropical Journal of Natural Product Research.
The manuscript discusses about the finding of flavonoid compound from sterculia quadrifida leaves. We first found the flavonoid compound from this plant. The compound have high antioxidant, anticancer dan antibacterial activity.

The manuscript has not been currently submitted for review to any other journal and will not be submitted elsewhere before a decision is made by this journal. We look forward for your positive response.

Kind regards

Rollando, M.Sc.
Program of Pharmacy
Ma Chung University
65151 Malang
Indonesia

Re: Submited article

Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>
Tue 9/14/2021 4:53 AM
To:apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>

Dear Rollando,
Thank you for your submission to the Tropical Journal of Natural Product Research (www.tjnpr) https://www.scopus.com/sourceid/21100933230 SCOPUS , published by the University of Benin and Natural Product Research Group.

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: ***Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves***

Best regards

Abiodun

Professor Abiodun Falodun, PhD

Editor-in-Chief:
Tropical Journal of Natural Product Research (TJNPR)
Head, Natural Product Research Group, University of Benin
Email:editor.tjnpr@uniben.edu; editor.tjnpr@gmail.com
www.tjnpr.org **SCOPUS, SCImago SJR Q4 0.13**
https://www.scopus.com/sources.uri

Professor of Pharmaceutical Chemistry
Fellow, Fulbright (USA)
Deputy Vice-Chancellor (Academic) 2014-2016
Faculty of Pharmacy
University of Benin
Phone: +234-807-318-4488;
email: faloabi@uniben.edu; abiodun.falodun@fulbrightmail.org
Google Scholar Citations
SCOPUS https://www.scopus.com/authid/detail.uri?

https://orcid.org/0000-0003-2929-3305authorId=12794326500#top

University of Benin TJNPR SCOPUS Q4
www.uniben.edu www.tjnpr.org

2. Artikel dalam proses review

(14-9-2021)

Manuscript Under Peer-Review Process

Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>
Tue 9/14/2021 5:48 AM
To:apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>
Cc:w.Warsito@ub.ac.id <w.Warsito@ub.ac.id>;m.Masruri@ub.ac.id <m.Masruri@ub.ac.id>;Widodo.wid@ub.ac.id <Widodo.wid@ub.ac.id>

The manuscript submitted to the Tropical Journal of Natural Product Research https://www.scopus.com/sourceid/21100933230 SCOPUS by the corresponding author is undergoing the peer-review process.

Title: *Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves*

Journal: Tropical Journal of Natural Product Research www.tjnpr.org

Corresponding Author: Rollando Rollando

Co-authors: Warsito Warsito, Masruri Masruri, Nashi Widodo

Manuscript No: TJNPR JNE228ARN

If you have any objections, please contact the editorial office as soon as possible. If we do not hear from you, we will assume you agree with your co-authorship.

If you did not co-author this submission, please contact the corresponding author directly

Thank you very much.

Best regards

Abiodun

Professor Abiodun Falodun, PhD

Editor-in-Chief:
Tropical Journal of Natural Product Research (TJNPR)
Head, Natural Product Research Group, University of Benin
Email:editor.tjnpr@uniben.edu; editor.tjnpr@gmail.com
www.tjnpr.org **SCOPUS, SCImago SJR Q4 0.13**
https://www.scopus.com/sources.uri

Professor of Pharmaceutical Chemistry
Fellow, Fulbright (USA)
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Google Scholar Citations
SCOPUS https://www.scopus.com/authid/detail.uri?

https://orcid.org/0000-0003-2929-3305authorId=12794326500#top

University of Benin TJNPR SCOPUS Q4
www.uniben.edu www.tjnpr.org

3. Revisi pertama: accepted with moderate corrections (27-9-2021)

Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

Editorial decision on manuscript submitted

Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>
Mon 9/27/2021 5:47 AM
To:apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>

1 attachments (169 KB)
Provisional acceptance 236.pdf;

Dear Dr Rollando,

The manuscript submitted to the Tropical Journal of Natural Product Research www.tjnpr.org Q4 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 5 issue 10, 2021**.
Kindly acknowledge the receipt of the mail.

Title: Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from *Sterculia Quadrifida* Leaves

Authors: Rollando Rollando*, Warsito Warsito, Masruri Masruri, Nashi Widodo

Decision: Accepts with moderate corrections

Congratulations

Best regards

Abiodun

Professor Abiodun Falodun, PhD

Editor-in-Chief:
Tropical Journal of Natural Product Research (TJNPR)
Head, Natural Product Research Group, University of Benin
Email:editor.tjnpr@uniben.edu; editor.tjnpr@gmail.com
www.tjnpr.org **SCOPUS, SCImago SJR Q4 0.13**
https://www.scopus.com/sources.uri

Professor of Pharmaceutical Chemistry
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Google Scholar Citations
SCOPUS https://www.scopus.com/authid/detail.uri?

https://orcid.org/0000-0003-2929-3305authorId=12794326500#top

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Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

Tropical Journal of Natural Product Research

Official Journal of the Natural Product Research Group
Faculty of Pharmacy, University of Benin 300001, Benin City, Nigeria
Phone: +2348073184488, Email: editor.tjnpr@gmail.com; editor.tjnpr@uniben.edu; Website: www.tjnpr.org

ISSN: 2616-0684 (Print); 2616-0692 (Online), **DOI**: 10.26538/tjnpr, ISI IF: 0.562 (2017)
Abstracted/Indexed: Index Copernicus **ICV (2017): 59.83**, Open-J-Gate, EMBASE, EBSCO Host, WorldCat, AJOL, CrossRef (USA), JIF, NCBI (PubMed), CAS

SCOPUS indexed, SCImago SjR 0.13

Ref. No. 406801802226 DATE: 26th September 2021

Pharmacy Department, Faculty of Science and Technology, Ma Chung University, Malang 65151, Indonesia

Dear Dr. Rollando,

Provisional Acceptance letter for Article Manuscript Number TJNPR JNE236ARN
Title: Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from *Sterculia Quadrifida* Leaves
Authors: Rollando Rollando*, Warsito Warsito, Masruri Masruri, Nashi Widodo

I am pleased to inform you that your paper sent to the Tropical Journal of Natural Product Research has been reviewed and recommended for publication as a research article.

However, before the issues raised by the Reviewers are forwarded, to enable you revise your manuscript accordingly, please pay a publication charge of **$ USD270**. The actual publication of the paper will be in the upcoming issue (Vol 5 issue 10, 2021).

Please, the manuscript number (TJNPR ----) should be included in the bank transfer.

Congratulations.

The money should be remitted in favour of

Name of account:	Teamee Natural Product
Bank Name:	Guaranty Trust Bank Plc
Account Number:	0248808386.
Sort Code:	058044128
Swift code:	GTBINGLA
Address of Bank:	Uselu Lagos Road, Benin City, Edo State, Nigeria

Sincerely,

Professor Abiodun Falodun
Editor-in-Chief

4. Editor mengirim hasil review artikel

(21-10-2021)

Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

Review Comments

Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>
Thu 10/21/2021 1:21 PM
To:apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>

3 attachments (804 KB)
AX1-TJNPR-2021-M354 Reviewed 1.docx; AX2-TJNPR-2021-M354 Reviewed 2.docx; AX3-TJNPR-2021-M354 Reviewer 2.pdf;

Review Comments (Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves)

Editorial comments to authors

Table 1-4: Use recommended table format (No borders except for column headings and bottom border) for Table 2

For reference section: replace 'et al' with names of all contributing Authors in Ref no; 15, 16, 18, 20, 22, 23.

Poor Grammatical presentation. Please, manuscript should be submitted for English Language editing.

A declaration of the liability of the authors for claims relating to the content of this article should also be included when submitting the revised manuscript. This should be stated as follows;
Authors' Declaration
The authors hereby declare that the work presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

All comments/corrections made by reviewers should be completely addressed, point by point, and make appropriate changes in the manuscript, or provide a suitable rebuttal to any specific request for change that has not been made.
All corrections/changes made in the manuscript should be **highlighted in yellow colour** when submitting the manuscript in the revised form on or before 2nd of November 2021

The authors should carefully revise and correct the manuscript taking into consideration the comments of all the reviewers. 50% of the references cited should be between 2016-2020. The revised and corrected manuscript should be subjected to plagiarism checker (17% allowed in TJNPR) and English language editing. Evidence of the checks should be attached when submitting the revised/corrected manuscript.
During submission of the revised manuscript include another file labelled "**Responses to reviewers' comments**" (a matrix) clearly showing your responses to each of the issues raised by the reviewers; mention the section, page and paragraph/lines where and how the changes/corrections have been made.

Strictly adhere to the author guidelines. Make sure that all the facts and information provided in the manuscript are correct. Check grammar, spelling, spacing, other information and facts including scientific names, formulae, symbols, equations, etc.

Ensure that all the references are correctly cited in the text and list. Verify all the references from their original sources. Confirm correctness of the citation info such as authors' names (surnames, initials, spelling, arrangements, etc), year, title, journal, volume, pages, punctuation, etc. The numbers and units must be presented according to the journal style. Use clearly distinguishable patterns for the illustrations/figures (e.g., graphs and charts) such that they should be legible even for black and white printing or when reduced in size.

Proofread the whole document after effecting all the corrections. The revised version should be approved by all the co-authors before submitting it.

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

Please find the attached review comments for your revisions.

Thank you very much for choosing the Tropical Journal of Natural Product Research.

Best regards

Abiodun

Professor Abiodun Falodun, PhD

Editor-in-Chief:
Tropical Journal of Natural Product Research (TJNPR)
Head, Natural Product Research Group, University of Benin
Email:editor.tjnpr@uniben.edu; editor.tjnpr@gmail.com
www.tjnpr.org **SCOPUS, SCImago SJR Q4 0.13**
https://www.scopus.com/sources.uri

Professor of Pharmaceutical Chemistry
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Deputy Vice-Chancellor (Academic) 2014-2016
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Google Scholar Citations
SCOPUS https://www.scopus.com/authid/detail.uri?

Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

REVIEW FORM

The Editorial Team of the Tropical Journal of Natural Product Research kindly request you to review the enclosed article. Please complete the form and return to the Editor-in-Chief, editor.tjnpr@gmail.com; editor.tjnpr@uniben.edu

A. MANUSCRIPT

Journal	**Tropical Journal of Natural Product Research**
Manuscript Number	TJNPR JNE228AR
Type of paper	Original Research
Title of paper	Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves
Name of Authors	

B. REVIEWER'S SPECIFIC COMMENTS PER SECTION OF MANUSCRIPT

Abstract	Abstract method and resume of result explain well but had Typo HLPC
Introduction	Introduction there many active sentences, e.g., "This genus is a rich source of flavonoids, steroids, alkaloids, saponins, triterpenoids, tannins, and phenols." It should be nice to write it with passive sentences, e.g.," genus had many secondary metabolite such as alkaloid, saponins, triterpenoid, tannins and phenol"
Methodology	Methodology was very clear My comment bellow 1. The author should be show equation antioxidant 2. Its very nice if brand of Material of solvent in HPLC explain clearly 3. The isolation material is new compound so author should be show methodology for show spectrogram UV Vis 4. Some species name not concern with binomial nomenclature eg Trichosanthes kirilowii, glucopyranosyloxy,
Results	Data of result was obvious, but have to show spectrogram UV Vis
Discussion	The discussion verry clear its will be nice if the author show chemical properties with simulation software for additional information Some typo eg Trichosanthes kirilowii, glucopyranosyloxy,
Conclusion	Conclusion was obvious
References	Conclusion was obvious
Figures, Tables	Conclusion was obvious

5. Author mengirimkan hasil revisi artikel

(26-10-2021)

Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

Re: Review comments

apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>
Tue 10/26/2021 5:55 AM
To:Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>

5 attachments (1 MB)
Plagiarism Report.doc; Responses to reviewers' comments.docx; Revised article-Marked.docx; Revised article-Unmarked.docx; Proofread Certificate.jpg;

To the Editor in Chief
Tropical Journal of Natural Product Research
Prof. Abiodun Falodun

I am the corresponding author of the article entitled "Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves".

Full authors: Rollando Rollando*, Warsito Warsito, Masruri Masruri, Nashi Widodo.

We have revised the article according to the feedback from the reviewers. We have flagged changes to the article.

Regards
Rollando Rollando

Prof. Abiodun Falodun

Editor in Chief

Tropical Journal of Natural Product Research

Dear Abiodun,

I would like to submit our revised manuscript entitles" **Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves"** for the consideration of publication in the tropical journal of natural product research.
I also have answered a point by point questions, comments and suggestions from the reviewer to improve our article quality as written along with this letter. I really appreciate for all these valuable comments and suggestions..

I hope very much that you would consider this manuscript for the publication in your esteemed journal. Your kind consideration would be gratefully acknowledged.

Thank you
Your sincerely

Rollando Rollando

Responses to reviewers' comments

Abstract method and resume of result explain well but had Typo HLPC	We have changed the HPLC typo, please check the abstract.
Introduction there many active sentences, e.g., "This genus is a rich source of flavonoids, steroids, alkaloids, saponins, triterpenoids, tannins, and phenols." It should be nice to write it with passive sentences, e.g.," genus had many secondary metabolite such as alkaloid, saponins, triterpenoid, tannins and phenol"	We have changed the sentence. Please check the changes on page 2 line 18-19.
The author should be show equation antioxidant	We have added equations for antioxidants. Kindly to check the addition at page 4 lines 86-87.
Its very nice if brand of Material of solvent in HPLC explain clearly	We have added brand material of solvent in hplc explain clearly. Kindly check these additions at page 3 line 43-44.
The isolation material is new compound so author should be show methodology for show spectrogram UV Vis	We have added UV/Vis spectra. Kindly to check these additional citations at page 6 line 135 and figure 1.
Some species name not concern with binomial nomenclature eg Trichosanthes kirilowii, glucopyranosyloxy,	We have changed the binomial nomenclature. Kondly check page 11 line 248 and page 12 line 269.
Table 1-4: Use recommended table format (No borders except for column headings and bottom border) for Table 2	We have changed the table format 1 to 4.
For reference section: replace 'et al' with names of all contributing Authors in Ref no; 15, 16, 18, 20, 22, 23.	We have fixed the reference.
Poor Grammatical presentation. Please, manuscript should be submitted for English Language editing.	We have fixed the grammatical error in the article.
A declaration of the liability of the authors for claims relating to the content of this article should also be included when submitting the revised manuscript. This should be stated as follows;Authors' Declaration: The authors hereby declare that the work presented in this article are original and that any liability for claims relating to the content of this article will be borne by them	We've added state to the Authors' Declaration. Kindly check page 12 lines 289-290.
50% of the references cited should be between 2016-2020.	We've fixed the reference. In this article 58% references between 2016-2020
The revised and corrected manuscript should be subjected to plagiarism checker (17% allowed in TJNPR) and English	We have detected our article on the plagiarism checker. Please check attachments.

language editing. Evidence of the checks should be attached when submitting the revised/corrected manuscript.	
Ensure that all the references are correctly cited in the text and list. Verify all the references from their original sources. Confirm correctness of the citation info such as authors' names (surnames, initials, spelling, arrangements, etc), year, title, journal, volume, pages, punctuation, etc. The numbers and units must be presented according to the journal style. Use clearly distinguishable patterns for the illustrations/figures (e.g., graphs and charts) such that they should be legible even for black and white printing or when reduced in size.	We have corrected the reference writing according to the article writing guide.

Plagiarism Checker X Originality Report

Similarity Found: 10%

Date: Saturday, October 23, 2021
Statistics: 344 words Plagiarized / 3330 Total words
Remarks: Low Plagiarism Detected - Your Document needs Optional Improvement.

Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves ABSTRACT Sterculia quadrifida is empirically used as a medicinal plant. The leaves of the plant are reported to have anti-infective, antioxidant, and anti-cancer activities. This study aims to identify active compounds from plant leaves by bioassay guided isolation. S.

quadrifida leaves were extracted with 80% methanol, then partitioned with n-hexane, chloroform, ethyl acetate, n-butanol, and insoluble n-butanol fractions by liquid-liquid partition. Purification of compounds using preparative HPLC and identification of structure were elucidated by comprehensive spectroscopic analyses. Aurone compounds were found, namely (2E)-2-[(3,4dihydroxyphenyl)(hydroxy)methylidene]-4,6-dihydroxy-2,3-dihydro-1 benzofuran-3-one which has the potential to be developed as an antibacterial, antioxidant, and cytotoxic compound. Keywords: Sterculia quadrifida, aurone, antibacterial, antioxidant, cytotoxic.

Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves

Rollando Rollando[1,2*], Warsito Warsito[3], Masruri Masruri[3], Nashi Widodo[4]

[1]Pharmacy Department, Faculty of Science and Technology, Ma Chung University, Malang 65151, Indonesia

[2]Doctoral Student, Chemistry Department, Faculty of Mathematics and Natural Sciences, Brawijaya University, Malang 65145, Indonesia

[3]Chemistry Department, Faculty of Mathematics and Natural Sciences, Brawijaya University, Malang 65145, Indonesia

[4]Biology Department, Faculty of Mathematics and Natural Sciences, Brawijaya University, Malang 65145, Indonesia

ABSTRACT

Sterculia quadrifida is empirically used as a medicinal plant. The leaves of the plant are reported to have anti-infective, antioxidant, and anti-cancer activities. This study aims to identify active compounds from plant leaves by bioassay guided isolation. *S. quadrifida* leaves were extracted with 80% methanol, then partitioned with n-hexane, chloroform, ethyl acetate, n-butanol, and insoluble n-butanol fractions by liquid-liquid partition. Purification of compounds using preparative HPLC and identification of structure were elucidated by comprehensive spectroscopic analyses. Aurone compounds were found, namely (2E)-2-[(3,4dihydroxyphenyl)(hydroxy)methylidene]-4,6-dihydroxy-2,3-dihydro-1 benzofuran-3-one which has the potential to be developed as an antibacterial, antioxidant, and cytotoxic compound.

***Keywords*:** *Sterculia quadrifida,* aurone, antibacterial, antioxidant, cytotoxic.

*Corresponding author. E mail: ro.llando@machung.ac.id

Tel: +6282220379864

6. Revisi kedua: Minor revisions

(10-11-2021)

Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

Revision to your Manuscript

Managing Editor TJNPR <p.editor.tjnpr@gmail.com>
Wed 11/10/2021 3:41 AM
To: apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>
Cc: Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>

1 attachments (420 KB)
TJNPR-2021-M354 Revised.docx;

Abstract: include a suitable conclusion.
Page 3, line 63-63; this is the final volume of solvent plus sample? What volume of methanol was used?
Page 3, line 75-78; rephrase for clarity.
Page 4, line 84,98; page 5, line 112; page 6, line 128,137; page 7, line 152; write equation using equation format.
Page 6, line 132-134,146-149; page 7, line 163; rephrase to correct grammatical error.
Include references for all methods.
Intext references should appear after punctuations (commas and full stops).
Table 3-4: confirm the values having commas that they are accurately reported. If they are, consider using mg/mL as unit instead for easy readability.

For reference section: include volume and issue numbers; ref 2,10,15,17,21,22,26.
Ref 6.8; write in English.
Ref 14; included page number.
Replace 'et al' with names of all contributing Authors in Ref no; 15, 16, 18, 20, 22, 23.

Submit the manuscript for English Language Editing.

7. Author mengirimkan hasil revisi artikel

(15-11-2021)

Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>
Mon 11/15/2021 3:07 PM
To:Managing Editor TJNPR <p.editor.tjnpr@gmail.com>
Cc:Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>

3 attachments (797 KB)
Responses to reviewers' comments.docx; TJNPR-2021-M354 Revised-Marked.docx; Proofread Certificate.jpg;

To the Editor in Chief
Tropical Journal of Natural Product Research
Prof. Abiodun Falodun

I am the corresponding author of the article entitled "Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves".

Full authors: Rollando Rollando*, Warsito Warsito, Masruri Masruri, Nashi Widodo.

We have revised the article according to the feedback from the reviewers. We have flagged changes to the article.

Regards
Rollando Rollando

Prof. Abiodun Falodun

Editor in Chief

Tropical Journal of Natural Product Research

Dear Abiodun,

I would like to submit our revised manuscript entitles" **Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from Sterculia Quadrifida Leaves"** for the consideration of publication in the tropical journal of natural product research.
I also have answered a point by point questions, comments and suggestions from the reviewer to improve our article quality as written along with this letter. I really appreciate for all these valuable comments and suggestions.

I hope very much that you would consider this manuscript for the publication in your esteemed journal. Your kind consideration would be gratefully acknowledged.

Thank you
Your sincerely

Rollando Rollando

Responses to reviewers' comments

Abstract: include a suitable conclusion.	Abstract writing has been improved. The research results have been written in the abstract (page 1-2; lines 22-27).
Page 3, line 63-63; this is the final volume of solvent plus sample? What volume of methanol was used?	In the extraction process using methanol. The volume of methanol used was 32 L. Corrected sentence to "The dried leaf powder (8.45 kg) was extracted using 32 L of 80% methanol" (page 4, line 69).
Page 3, line 75-78; rephrase for clarity.	Sentence writing has been corrected.
Page 4, line 84,98; page 5, line 112; page 6, line 128,137; page 7, line 152; write equation using equation format.	All sentences have been corrected and the equation has been written using equation format.
Page 6, line 132-134,146-149; page 7, line 163; rephrase to correct grammatical error. Include references for all methods.	The grammatical error has been fixed.
In text references should appear after punctuations (commas and full stops).	In text references have been corrected and written after punctuations (commas and full stops).
Table 3-4: confirm the values having commas that they are accurately reported. If they are, consider using mg/mL as unit instead for easy readability.	Table 3-4 has been fixed.
For reference section: include volume and issue numbers; ref 2,10,15,17,21,22,26.	Volume and issues on refs 2,10,15,17,21,22,26 have been added.
Ref 6.8; write in English.	Ref 6.8 has been written in english.
Ref 14; included page number.	Ref 14 has been written page number.
Replace 'et al' with names of all contributing Authors in Ref no; 15, 16, 18, 20, 22, 23.	et al were removed in Ref no; 15, 16, 18, 20, 22, 23.

Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

8. Manajer editor mengirimkan galley proof

(2-12-2021)

Dr. apt. Rollando, S.Farm., M.Sc.
Pengajuan ke Lektor Kepala

Galley Proof of Your Article

Managing Editor TJNPR <p.editor.tjnpr@gmail.com>
Thu 12/2/2021 4:05 AM
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Find attached the galley proof of your article titled "**Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from *Sterculia Quadrifida* Leaves**"

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Original Research Article

Antibacterial, Antioxidant, and Cytotoxic Flavonoid Compound from *Sterculia Quadrifida* Leaves

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ABSTRACT

Sterculia quadrifida is empirically used as a medicinal plant. The leaves of the plant are reported to have anti-infective, antioxidant, and anti-cancer activities. This study aims to identify active compounds from the plant leaves by bioassay-guided isolation. *S. quadrifida* leaves were extracted with 80% methanol, then partitioned with n-hexane, chloroform, ethyl acetate, n-butanol, and insoluble n-butanol fractions by liquid-liquid partition. Purification of compounds was done using preparative HPLC, identification and structure elucidation were by comprehensive spectroscopic analyses. The *in vitro* antioxidant assay of the isolated compound was investigated using the 1,1-diphenyl-2-picrylhydrazyl (DPPH), 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS), nitric oxide (NO), and hydrogen peroxide (H_2O_2) radical scavenging methods. The *in vitro* antibacterial assay was done using the microdilution method. The *in vitro* cytotoxic effect of the compound was investigated using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The isolation results from the n-butanol fraction found a new aurone compound named (2E)-2-[(3,4-dihydroxy phenyl)(hydroxy)methylidene]-4,6-dihydroxy-2,3-dihydro-1-benzofuran-3-one. The antioxidant assay results showed IC_{50} values of 46.36, 38.41, 37.85, and 20.50 µg/mL in the DPPH, ABTS, NO, and H_2O_2 assays, respectively. The antibacterial assay results showed IC_{50} values of 23.38, 26.22, 58.45, 100.92, 103.14, and 193.98 µg/mL against *P. aureginosa*, *H. pylori*, *S. bovis*, *S. aureus*, *S. thypi*, *E. coli*, respectively. The cytotoxicity assay showed IC_{50} values of 4.05, 12.53, 15.38, and 25.91 µg/mL against breast cancer cell lines (4T1, MCF7, MDA-MB-435, and T47D). The aurone compound could be developed as a potential antibacterial, antioxidant, and cytotoxic agent.

Keywords: *Sterculia quadrifida,* aurone, antibacterial, antioxidant, cytotoxic.

Introduction

The genus Sterculia generally grows in the tropics and sub-tropics.[1] the genus had many secondary metabolites such as alkaloids, saponins, triterpenoids, tannins, and phenolics.[2] Several species in this genus are traditionally used to treat ulcers, diarrhoea, fever, stroke, diabetes, and inflammation.[3] *Sterculia quadrifida*, a plant called "Faloak" in Indonesia, has a significant role in folk medicine, especially for infectious diseases, as anti-hepatitis, and anticancer.[4] However, studies of *S. quadrifida* plants are still limited. Only a few studies have been conducted in the last decade investigating the phytochemical content of *S. quadrifida* plants and isolating triterpenoids and anthraquinone compounds.[5,6] Some of these compounds show pharmacological effects, such as anti-hepatitis[7], immunostimulant, antioxidant, anti-cancer, and antibacterial activities.[7-9] Among all compounds, flavonoids have the potential to be used as anti-infective, antioxidant, and anti-cancer agent.[10] Therefore, this study aimed to isolate the active antibacterial, antioxidant, and anti-cancer compounds from the methanol leaves extract of *S. quadrifida* using chromatographic techniques.

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Materials and Methods

General
1D and 2D NMR data are collected on JEOL JNM-ECZR 500 MHz instruments with DMSO as internal standard. The IR spectra were recorded on Jasco FT/IR-6800 type A. LC-MS/MS data were obtained using Shimadzu LCMS-8045. Isolation of the compound was done using Sykam S 723 HPLC Preparative with ACE®-C18 column (1cm-10x250 mm), 1.5 mL/min. The TLC was carried out on precoated silica gel 60 F_{254} (Merck), then the plate was analyzed under UV light. Merck and HPLC grades solvents used were acetonitrile, methanol, n-butanol, chloroform, ethyl acetate, and n-hexane.

Plant material
Sterculia quadrifida was collected from Kupang City, East Nusa Tenggara, Indonesia in January 2020. Botanist Dr Budi Sumatra authenticated the plant samples. Voucher specimen (FA:023-MACHUNG-2020) was deposited in the Pharmacognosy Laboratory, Department of Pharmacy, Ma Chung University.

Extraction and isolation
The dried leaf powder (8.45 kg) was extracted using 32 L of 80% methanol. The crude extract was concentrated, and 798.21 g of extract was obtained. The extract was dissolved in 80% methanol and partitioned by solvent-solvent extraction using n-hexane, ethyl acetate, chloroform, and n-butanol. Each fraction was tested for antibacterial, antioxidant, and cytotoxic activity using the concept of bioassay-guided isolation. The test results showed that the n-butanol fraction was the most active. Then, the n-butanol fraction (150 g) was purified