

### **Bukti Korespondensi**

**Judul Artikel: In vitro Cytotoxic Potential of Sterculia quadrifida Leaf Extract Against Human Breast Cancer Cell Lines**

<b>No</b>	<b>Proses</b>	<b>Tanggal</b>
1	Artikel di ajukan ke jurnal <i>Tropical Journal of Natural Product Research</i>	15-7-2022
2	Revisi pertama: <i>accepted with moderate corrections</i>	23-7-2022
3	Editor mengirim hasil review artikel • Review form	28-7-2022
4	Author mengirimkan hasil revisi artikel • Response to reviewer • Plagiarism check • Revised article	29-7-2022
5	Revisi kedua: Minor revisions	19-8-2022
6	Author mengirimkan hasil revisi artikel • Response to reviewer • Plagiarism check • Revised article	26-8-2022
7	Manajer Editor meminta "Proofreading"	28-8-2022
8	Author mengirimkan hasil "Proofreading"	30-8-2022
9	Manajer editor mengirimkan <i>galley proof</i>	1-9-2022
10	Author mengirimkan kembali kepada manajer editor hasil revisi <i>galley proof</i>	1-9-2022
11	Artikel dipublikasi pada <i>Tropical Journal of Natural Product Research</i> . Vol. 6. Issue 8. September 2022	2-9-2022

- 1. Artikel di ajukan ke jurnal *Tropical Journal of Natural Product Research*  
(15-7-2022)**

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

**Submitted Manuscript**

apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>

Fri 7/15/2022 6:07 AM

To:Editor-in-Chief Tjnpr <editor.tjnpr@gmail.com>;Managing Editor TJNPR <p.editor.tjnpr@gmail.com>

 7 attachments (701 KB)

Abstract.docx; Authors Contributor.docx; Cover latter.doc; DECLARATION AND COPYRIGHT TRANSFER FORM.docx; Main Manuscript\_Submitted.docx; Plagiarism Checker.pdf; Potential Reviewer.docx;

Dear Prof. **Abiodun** Falodun, PhD

I am herewith submitting the manuscript entitled "In Vitro Cytotoxic Potential of Sterculia Quadrifida Leaves Against Human Breast Cancer Cell Lines ." for publication in Tropical Journal of Natural Product Research.

In this paper, we report on Sterculia quadrifida is a plant that has anti-cancer potential. In this research we first report the anti-cancer activity from leaves. This is significant because there is little information about the exploration of medicinal plants of Sterculia quadrifida. The paper should be of interest to readers in the areas of Pharmacognosy, phytochemistry, and breast cancer research.

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

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

Re: Submitted Manuscript

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

Fri 7/15/2022 4:41 PM

To: apt. Rollando, S.Farm, M.Sc. <ro.llando@machung.ac.id>

Dear Dr Rollando,

Thank you for submitting your original manuscript to the Tropical Journal of Natural Product Research ([www.tjnpr.org](http://www.tjnpr.org)) <https://www.scopus.com/sourceid/21100933230> SCOPUS <sub>Q4</sub> 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.

Title: ***In Vitro* Cytotoxic Potential of Sterculia Quadrifida Leaves Against Human Breast Cancer Cell Lines**

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](mailto:editor.tjnpr@uniben.edu); [editor.tjnpr@gmail.com](mailto:editor.tjnpr@gmail.com)

[www.tjnpr.org](http://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](mailto:faloabi@uniben.edu); [abiodun.falodun@fulbrightmail.org](mailto:abiodun.falodun@fulbrightmail.org)

[Google Scholar Citations](https://scholar.google.com/citations?hl=en&user=faloabi)

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TROPICAL JOURNAL of  
NATURAL  
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[www.uniben.edu](http://www.uniben.edu)

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**2. Revisi pertama: accepted with moderate corrections**  
**(23-7-2022)**

**Dr. apt. Rollando, S.Farm., M.Sc.**

Pengajuan ke Lektor Kepala

Editorial decision on manuscript submitted for publication in TJNPR

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

Sat 7/23/2022 2:37 PM

To: apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>

1 attachments (201 KB)

Provisional acceptance 173.pdf;

Dear Dr. Rollando,

The manuscript submitted to the Tropical Journal of Natural Product Research [www.tjnpr.org](http://www.tjnpr.org) <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 6 issue 7, 2022.

Kindly acknowledge the receipt of the mail.

**Title:** *In Vitro* Cytotoxic Potential of *Sterculia Quadrifida* Leaves Against Human Breast Cancer Cell Lines

**Authors:** Rollando Rollando\*, Eva Monica, Muhammad Hilmi Aftoni

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](mailto:editor.tjnpr@uniben.edu); [editor.tjnpr@gmail.com](mailto:editor.tjnpr@gmail.com)

[www.tjnpr.org](http://www.tjnpr.org) **SCOPUS, SCImago SJR Q4 0.13**

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Professor of Pharmaceutical Chemistry

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Phone: +234-807-318-4488;

email: [faloabi@uniben.edu](mailto:faloabi@uniben.edu); [abiodun.falodun@fulbrightmail.org](mailto:abiodun.falodun@fulbrightmail.org)

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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](mailto:editor.tjnpr@gmail.com); [editor.tjnpr@uniben.edu](mailto:editor.tjnpr@uniben.edu); Website: [www.tjnpr.org](http://www.tjnpr.org)

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SCOPUS indexed, SCImago SJR 0.13

Ref. No. 406801802223

DATE: 23rd July, 2022

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

Dear Dr. Rollando,

**Provisional Acceptance letter for Article Manuscript Number TJNPR JNE173ARN**

Title: In Vitro Cytotoxic Potential of *Sterculia Quadrifida* Leaves Against Human Breast Cancer Cell Lines

Authors: Rollando Rollando\*, Eva Monica, Muhammad Hilmi Aftoni

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 6 issue 7, 2022**).

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**

**3. Editor mengirim hasil review artikel**  
**(28-7-2022)**



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

## Review Comments

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

Thu 7/28/2022 10:00 AM

To: apt. Rollando, S.Farm, M.Sc. <ro.lando@machung.ac.id>

5 attachments (1 MB)

IVC1-TJNPR-2022-M236 Reviewed 1.docx; IVC2-TJNPR-2022-M236 Reviewed 2.docx; IVC3-TJNPR-2022-M236 Reviewed 3.docx; IVC4-TJNPR-2022-M236 Reviewer 1.docx; IVC5-TJNPR-2022-M236 Reviewer 2.pdf;

Review Comments (In Vitro Cytotoxic Potential of Sterculia Quadrifida Leaves Against Human Breast Cancer Cell Lines)

### Editorial comments to authors

Include weight of plant sample used in maceration process.

Materials and Methods: Include section for statistical analysis.

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

For reference section: replace 'et al' with names of all contributing authors for Ref. no; 2, 5, 6, 10-12, 14, 15, 21, 24.

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 30th July 2022**

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](mailto:editor.tjnpr@uniben.edu); [editor.tjnpr@gmail.com](mailto:editor.tjnpr@gmail.com)

[www.tjnpr.org](http://www.tjnpr.org) **SCOPUS, SCImago SJR Q4 0.13**

<https://www.scopus.com/sources.uri>

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



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**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](mailto:editor.tjnpr@gmail.com); [editor.tjnpr@uniben.edu](mailto:editor.tjnpr@uniben.edu)

**A. MANUSCRIPT**

Journal	<b>Tropical Journal of Natural Product Research</b>
Manuscript Number	
Type of paper	Original article
Title of paper	In Vitro Cytotoxic Potential of Sterculia Quadrifida Leaves Against Human Breast Cancer Cell Lines
Name of Authors	TJNPR JNE173AR

**B. REVIEWER'S SPECIFIC COMMENTS PER SECTION OF MANUSCRIPT**

Abstract	Well written abstract
Introduction	The introduction is written in full
Methodology	Complete written method
Results	All research data has been discussed
Discussion	All research data has been discussed
Conclusion	Well written conclusion
References	All references have been cited
Figures, Tables	Figures and tables are written correctly

**D. REVIEWER'S RECOMMENDATION**

Please mark with "X" one of the options.

You state the article should:

Publish as it is	
Accept with minor revisions (editor will check), specific comments to the editor below	X
Accept with moderate revisions as recommended by reviewer	
Accept with major corrections (the article should be thoroughly changed)	
<b>Full article</b>	X
<b>Short communication</b>	
Reject for reasons noted by the reviewer (please be specific)	

**E. REVIEWER'S INFORMATION**



**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](mailto:editor.tjnpr@gmail.com); [editor.tjnpr@uniben.edu](mailto:editor.tjnpr@uniben.edu)

**A. MANUSCRIPT**

Journal	<b>Tropical Journal of Natural Product Research</b>
Manuscript Number	TJNPR JNE173AR
Type of paper	Research paper
Title of paper	In Vitro Cytotoxic Potential of Sterculia Quadrifida Leaves Against Human Breast Cancer Cell Lines
Name of Authors	

**B. REVIEWER'S SPECIFIC COMMENTS PER SECTION OF MANUSCRIPT**

Abstract	Abstract written clearly
Introduction	Introduction written clearly
Methodology	Methodology written clearly
Results	Research results are written clearly
Discussion	Should be added a theory that explains the role of secondary metabolites on anticancer.
Conclusion	Conclusion are written clearly
References	References written clearly
Figures, Tables	Figures and tables have been cite

**D. REVIEWER'S RECOMMENDATION**

Please mark with "X" one of the options.

You state the article should:

Publish as it is	
Accept with minor revisions (editor will check), specific comments to the editor below	
Accept with moderate revisions as recommended by reviewer	✓
Accept with major corrections (the article should be thoroughly changed)	
<b>Full article</b>	✓
<b>Short communication</b>	
Reject for reasons noted by the reviewer (please be specific)	

- 4. Author mengirimkan hasil revisi artikel  
(29-7-2022)**


**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>

Fri 7/29/2022 3:27 PM

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

 2 attachments (361 KB)

Main Manuscript\_Revised.docx; Responses to reviewers' comments.docx;

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

Dear Abiodun,

I would like to submit our revised manuscript entitles "**In Vitro Cytotoxic Potential of Sterculia Quadrifida Leaves Against Human Breast Cancer Cell Lines**" 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 all these valuable comments and suggestions.

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

Thank you  
Your sincerely

Rollando Rollando

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

Prof. Abiodun Falodun

Editor in Chief

Tropical Journal of Natural Product Research

Dear Abiodun,

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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**

Include weight of plant sample used in maceration process.	The data has been added. Page 4, sentence numbers 72-73.
Materials and Methods: Include section for statistical analysis.	The data has been added. Page 6, sentence number 126-130.
Table 1-2: Use recommended table format (No borders except for column headings and bottom border)	The table has been fixed
For reference section: replace 'et al' with names of all contributing authors for Ref. no; 2, 5, 6, 10-12, 14, 15, 21, 24.	It's been clarified
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.	Already added
Discussion should be added, especially the theory section.	Discussion has been added

125

126 *Statistical Analysis*

127 The results were expressed as mean  $\pm$  standard deviation of mean (SD), and statistical  
128 comparisons were made using one-way analysis of variance (ANOVA) to test the null  
129 hypothesis. Tukey's test was done to compare the sample means. The data were considered  
130 significantly different from other fraction when significance level was  $p < 0.05$ .

131

132 **Result and Discussion**

133 Cytotoxic tests were carried out on several breast cancer cells, namely T47D, MCF-7, 4T1,  
134 and MDA-MB-231 cells. The test method used is the MTT method. This is a colorimetric  
135 method where the MTT reagent is a tetrazolium salt that can be broken down into formazan  
136 crystals by the succinate tetrazolium reductase system found in the cellular respiration pathway

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227 young adult cancer patients' needs. J Adolesc Young Adult Oncol. 2021; 10(2): 105–108.

228 2. Miura S, Naito T, Mitsunaga S, Omae K, Mori K, Inano T, Yamaguchi T, Tatematsu N,  
229 Okayama T, Morikawa A, Mouri T, Tanaka H, Kimura M, Imai H, Mizukami T, Imoto A,  
230 Kondoh C, Shiotsu S, Okuyama H, Ueno M, Takahashi T, Tsuji T, Aragane H, Inui A,

10

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231 Higashiguchi T, Takayama K. A randomized phase II study of nutritional and exercise  
232 treatment for elderly patients with advanced non-small cell lung or pancreatic cancer: the  
233 NEXTAC-TWO study protocol. BMC Cancer. 2019; 19(3):528.



**5. Revisi kedua: Minor revisions**  
**(19-8-2022)**

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

### Revision to your Manuscript

Managing Editor TJNPR <p.editor.tjnpr@gmail.com>

Fri 8/19/2022 11:48 AM

To: apt. Rollando, S.Farm, M.Sc. <ro.llando@machung.ac.id>

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

1 attachments (375 KB)

TJNPR-2022-M236 Revised.docx;

Abstract: the methodology has not been properly summarized. Also, include a suitable conclusion.

Page 3, line 1-5; introduction should end by stating the aim of the study.

Include details of the authentication of the plant sample.

Page 4, line 2; how was it reduced in size?

Page 4, line 10; page 5, line 2; state the meaning of abbreviations at the first mention.

Page 5,6; include reference for the formula.

Include volume of solvent used in maceration process.

Page 9, line 1-8; rephrase to correct grammatical errors.

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

**For reference section:** include volume, issue and page numbers; ref 5,8,10,11,18,20,26,

**Ref 18; include name of the journal.**

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

**6. Author mengirimkan hasil revisi artikel  
(26-8-2022)**


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

**Re: Revision to your Manuscript**

Dr. apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>

Fri 8/26/2022 4:53 PM

To:Managing Editor TJNPR <p.editor.tjnpr@gmail.com>

 2 attachments (367 KB)

Responses to reviewers' comments.docx; TJNPR-2022-M236 Revised.docx;

Dear Managing Editor TJNPR

Here i attach the revision of my article, i also include response of review.

Regards

---

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

Prof. Abiodun Falodun

Editor in Chief

Tropical Journal of Natural Product Research

Dear Abiodun,

I would like to submit our revised manuscript entitled” **In Vitro Cytotoxic Potential of Sterculia Quadrifida Leaves Against Human Breast Cancer Cell Lines**” 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: the methodology has not been properly summarized. Also, include a suitable conclusion.	We have fixed.
Page 3, line 1-5; introduction should end by stating the aim of the study.	We've state the aim of the study
Include details of the authentication of the plant sample.	We have fixed
Page 4, line 2; how was it reduced in size?	We have state the process to reduced the size
Page 4, line 10; page 5, line 2; state the meaning of abbreviations at the first mention.	We have fixed reference writing. All citations have been confirmed to be in the bibliography.
Page 5,6; include reference for the formula.	We've fixed the reference
Include volume of solvent used in maceration process.	We've include the volume of the solvent
Page 9, line 1-8; rephrase to correct grammatical errors.	We've fixed the reference
Table 1-2: Use recommended table format (No borders except for column headings and bottom border)	We've fixed the table
For reference section: include volume, issue and page numbers; ref 5,8,10,11,18,20,26,	We've fixed the reference
Ref 18; include name of the journal.	We've fixed the reference

1 **In Vitro Cytotoxic Potential of Sterculia Quadrifida Leaves Against Human Breast Cancer**

2 **Cell Lines**

3 Rollando Rollando<sup>1\*</sup>, Eva Monica<sup>1</sup>, Muhammad Hilmi Aftoni<sup>1</sup>

4 <sup>1</sup>Pharmacy Department, Faculty of Science and Technology, Ma Chung University, Malang

5 65151, Indonesia

6

7 **ABSTRACT**

8 *Sterculia quadrifida* R.Br is used empirically by the people of East Nusa Tenggara as a  
9 medicinal plant. This study aims to determine the potential of the fraction resulting from the  
10 ethanol extract of the leaves of *S. quadrifida* as an anti-breast cancer agent. Extraction using  
11 maceration method with ethanol solvent (80%), then fractionation with liquid-liquid partition,  
12 and cytotoxic test using MTT method. Cytotoxic test results showed that the ethyl acetate

186 acetate fraction had cytotoxic activity in MCF-7 with IC<sub>50</sub> of 7.62 µg/mL while the selectivity  
187 index was 2.52.<sup>24</sup>

188 Isolation of cytotoxic compounds from *S. quadrifida* found derivatives of naphthoquinone  
189 compounds, namely 2,3-dihydro-6-hydroxy-2-methylenenaphtho[1,2-b] furan - 4.5-dione that  
190 has anticancer activity with IC<sub>50</sub> 9.88 g/ mL and a selectivity index value of 30.23 in cancer cells  
191 T47D.<sup>25</sup> Isolate compound namely 2- iminoethyl 2-(2-(1-hydroxypentan-2-yl)phenyl) acetate  
192 from ethyl acetate fraction had cytotoxic activity against T47D breast cancer cells with IC<sub>50</sub> 7.12  
193 µg/mL and selectivity index value of 47.53.<sup>26</sup> In addition, auron compound has been isolated in  
194 n-butanol fraction named (2E)-2-[(3,4-dihydroxy phenyl)(hydroxy)methylidene]-4,6-dihydroxy-  
195 2,3-dihydro-1-benzofuran-3-one with IC<sub>50</sub> in 4T1 cells of 4.05 µg/mL.<sup>27</sup>

196 Compounds that have been isolated from the plant *S. quadrifida* are naphthoquinone and  
197 auron compounds. In several studies, naphthoquinone compounds have shown cytotoxic activity

**7. Manajer Editor meminta “Profreading”  
(28-8-2022)**




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

## Re: Revision to your Manuscript

Managing Editor TJNPR <p.editor.tjnpr@gmail.com>

Sun 8/28/2022 2:26 AM

To:Dr. apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>

 1 attachments (375 KB)

TJNPR-2022-M236 Revised 2.docx;

Submit the manuscript for English Language editing.

**8. Author mengirimkan hasil “Proofreading”  
(30-8-2022)**

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

**Re: Revision to your Manuscript**

Dr. apt. Rollando , S.Farm, M.Sc. <ro.llando@machung.ac.id>

Tue 8/30/2022 8:35 AM

To:Managing Editor TJNPR <p.editor.tjnpr@gmail.com>

 2 attachments (1 MB)

Edited Manuscript of Rollando Rollando.doc; Proofreading Certificate (Rollando Rollando).pdf;

Dear Managing Editor TJNPR

I attach a proofreading article and a proofreading certificate. Hopefully it can be processed properly for publication.

Regards

---

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



10 **ABSTRACT**

11 Breast cancer is the most common type of cancer among women worldwide. The main  
12 treatments for breast cancer are surgery and chemotherapy, but the medications used are  
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**11. Artikel dipublikasi pada *Tropical Journal of Natural Product Research*. Vol. 6. Issue 8. September 2022**

**(2-9-2022)**



**In vitro Cytotoxic Potential of *Sterculia quadrifida* Leaf Extract Against Human Breast Cancer Cell Lines**

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ABSTRACT

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Breast cancer is the most common type of cancer among women worldwide. The main treatments for breast cancer are surgery and chemotherapy, but the medications used are associated with several side effects. *Sterculia quadrifida* R. Br is traditionally used by the people of East Nusa Tenggara as a medicinal plant to treat various diseases. This study was conducted to determine the potential of the ethanol fraction of *S. quadrifida* leaf extract as an anti-breast cancer agent. Human breast cancer cell lines (MCF-7, T47D, 4T1, MDA-MB-231, and Vero) were obtained for the study. An ethanol solvent (80%) was employed to extract the leaves of *S. quadrifida* using the maceration method. The *S. quadrifida* leaf extract was then fractionated with n-hexane, ethyl acetate, and n-butanol with a liquid-liquid partition. An *in vitro* cytotoxicity assay was conducted on the MCF-7, T47D, 4T1, MDA-MB-231, and Vero cells using the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide) method. The results showed that the ethyl acetate fraction of the *S. quadrifida* leaf extract exhibited considerable cytotoxic activity in T47D and 4T1 breast cancer cells, with an IC<sub>50</sub> value of 19.86 ± 3.48 and 16.70 ± 3.33 µg/mL, respectively. Furthermore, the n-hexane fraction had the highest activity in MCF-7 cells with an IC<sub>50</sub> value of 33.78 ± 7.82 µg/mL. The findings of this study revealed that the leaves of *S. quadrifida* have the potential to act as a cytotoxic agent on breast cancer cells.

**Keywords:** Breast cancer, Cytotoxic, Leaf extract, MTT assay, *Sterculia quadrifida*

Introduction

Cancer in recent decades has become a major concern in the health sector.<sup>1</sup> This is attributable to the increasing prevalence of cancer in several developing and developed countries.<sup>2</sup> Breast cancer ranks first in cancer cases in women worldwide, with an incidence rate of 1.6 million.<sup>3</sup> It is the leading cause of cancer death in women.<sup>4</sup> Breast cancer is classified into four major molecular subtypes: luminal A (HR+/HER2-), luminal B (HR+/HER2+), HER2+, and triple-negative. Each of them has its own set of risk factors for incidence, disease progression, preferred organ locations of metastases, and therapeutic response.<sup>5</sup> Although surgery and chemotherapy are the primary treatments for breast cancer, selective medications are still required to improve efficacy, and selectivity, and reduce side effects.<sup>6</sup> The use of natural products in cancer therapy is increasing rapidly at the moment, owing to the belief that conventional medications have frequent negative effects.<sup>7</sup> Many researchers have been inspired to investigate plants and secondary metabolites with anti-breast cancer activities. Taxol compounds, for example, are terpenoid compounds identified from *Taxus brevifolia* as the first microtubule stabilizing agents that interact molecularly with the hydrophobic pocket in the β-tubule.<sup>8</sup> Scientific evidence shows that *Catharanthus roseus* produces vinblastine and vincristine chemicals via a mechanism involving α, and β-tubulins.<sup>9</sup> Furthermore, luteolin, a flavone found in *Salvia tomentosa* Mill., has been shown to delay or block the development of cancer cells, protect DNA from a carcinogenic stimulus, and induce apoptosis even in multidrug-resistant cancer cells.

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This is achieved through reactive oxygen species (ROS) generation, DNA damage, activation of ataxia telangiectasia and rad3-related/checkpoint kinase 2/p53 (ATR/Chk2/p53) signaling, depletion of antiapoptotic proteins and inhibition of NF-κB signaling and p38.<sup>10</sup> Furthermore, the natural product is thought to have significant cytotoxic potential.<sup>11</sup> This study was aimed at investigating the potential of *S. quadrifida* leaf extract as a cytotoxic agent in breast cancer cells.

Materials and Methods

Source of cell lines

The MCF-7, T47D, 4T1, MDA-MB-231, and Vero cells were obtained from the American Type Culture Collection (Manassas, USA). Briefly, cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) (Gibco, USA) supplemented with 10% (v/v) foetal bovine serum (FBS) (Gibco, USA), 150 IU/mL penicillin, 150 µg/mL streptomycin (Gibco, USA) and 12.5 µg/mL amphotericin B (Gibco, USA).

Source and identification of plant material

The leaves of *S. quadrifida* were collected in January 2022 at the Research and Development Center for Environment and Forestry, Kupang, East Nusa Tenggara, Indonesia. The collection locations are S 10° 07' 40"-10°17' 39" and E 123° 31' 35"-123° 41' 00". Kupang City has a low average annual rainfall (1,290 mm/year). The average humidity is 77%, and the average temperature is 27.5°C. The plant was identified at the Laboratory of Herbal Materia Medica Batu, Indonesia. The root, stem, and leaf parts of the plant were authenticated using the Flora of Java book. The remaining plant sample was labeled as *Sterculia quadrifida* and deposited in the Pharmacognosy-Phytochemical Laboratory of Ma Chung University, Indonesia with a voucher number: FA:023-MACHUNG-2022.