

### **Bukti Korespondensi**

**Judul Artikel: *Sterculia foetida* Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: In-Vitro and In-Silico Studies.**

<b>No</b>	<b>Proses</b>	<b>Tanggal</b>
1	Artikel di ajukan ke jurnal <i>Tropical Journal of Natural Product Research</i>	6-12-2020
2	Editor meminta rekomendasi tiga orang yang memiliki potensi untuk menjadi reviewer artikel	6-12-2020
3	Artikel dalam proses review	7-12-2020
4	Revisi pertama: <i>accepted with moderate corrections</i>	23-12-2020
5	Editor mengirim hasil review artikel <ul style="list-style-type: none"><li>• Review form</li></ul>	25-12-2020
6	Author mengirimkan hasil revisi artikel <ul style="list-style-type: none"><li>• Response to reviewer</li><li>• Plagiarism check</li><li>• Revised article</li></ul>	9-1-2021
7	Manajer editor mengirimkan <i>galley proof</i>	2-2-2021
8	Author mengirimkan kembali kepada manajer editor hasil revisi <i>galley proof</i>	3-2-2021
9	Artikel dipublikasi pada <i>Tropical Journal of Natural Product Research</i> . Vol. 5. Issue 1. Februari 2021	3-2-2021

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

**1. Artikel di ajukan ke jurnal *Tropical Journal of Natural  
Product Research*  
(6-12-2020)**

**Submit Manuscript\_Rollando**

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

Sun 12/6/2020 1:43 PM

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

Cc:rollando2008@gmail.com <rollando2008@gmail.com>

 6 attachments (7 MB)

Abstract.docx; Cover latter.doc; DECLARATION AND COPYRIGHT TRANSFER FORM.docx; Manuscript\_Rollando.docx; Supplementary Materials.docx;  
Manuscript\_Rollando.pdf;

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

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

**2. Editor meminta rekomendasi tiga orang yang memiliki  
potensi untuk menjadi reviewer artikel  
(6-12-2020)**

Re: Submit Manuscript\_Rollando

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

Sun 12/6/2020 1:56 PM

To: apt. Rollando, S.Farm, M.Sc. <ro.rollando@machung.ac.id>  
Cc: rollando2008@gmail.com <rollando2008@gmail.com>

Dear Dr Rollando,

Thank you for submitting your original article for publication in the Tropical Journal of Natural Product Research ([www.tjnpr](http://www.tjnpr)) <https://www.scopus.com/sourceid/21100933230> SCOPUS Q3

Kindly send the names, affiliation and VALID email addresses of three potential reviewers, two from your country and the other from outside your country. The email addresses of the co-authors are also needed, stating also their roles in the study.

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

**3. Artikel dalam proses review**  
**(7-12-2020)**

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

Pengajuan ke Lektor Kepala

**Manuscript Under Peer-Review Process**

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

Mon 12/7/2020 4:35 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 Q3 by the corresponding author is undergoing the peer-review process.

Title: *Sterculia foetida* Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: *In-Vitro* and *In-Silico* Study

Journal: Tropical Journal of Natural Product Research [www.tjnpr.org](http://www.tjnpr.org)

Corresponding Author: Rollando Rollando

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

Manuscript No: TJNPR JAN708ARN

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

The editorial decision will be communicated as soon as the review process is completed.

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

[www.tjnpr.org](http://www.tjnpr.org) **SCOPUS, SCImago SJR Q3 0.13**

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

Professor of Pharmaceutical Chemistry

Fellow, Fulbright (USA)

Deputy Vice-Chancellor (Academic) 2014-2016

Faculty of Pharmacy

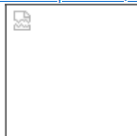
University of Benin

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](#)

SCOPUS <https://www.scopus.com/authid/detail.uri?authorId=12794326500#top>



University of Benin TJNPR **SCOPUS Q3**

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[www.tjnpr.org](http://www.tjnpr.org)

**4. Revisi pertama: accepted with moderate corrections  
(23-12-2020)**



**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>

Wed 12/23/2020 10:59 PM

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

1 attachments (170 KB)

Provisional acceptance 708.pdf;

Dear Dr Rollando,

The manuscript submitted to the Tropical Journal of Natural Product Research [www.tjnpr.org](http://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 5 issue 1, January 2021**.

Kindly acknowledge the receipt of the mail.

**Title:** *Sterculia foetida* Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: In-Vitro and *In-Silico* Study

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

TJNPR Editorial Decision: accepted with moderate corrections

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)

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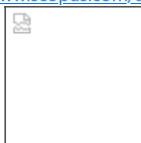
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[Google Scholar Citations](https://scholar.google.com/citations?hl=en&user=faloabi)

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Dr. apt. Rollando, S.Farm., M.Sc.  
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## 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)

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. 406801245715

DATE: 23<sup>rd</sup> December 2020

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

Dear Dr Rollando,

### **Provisional Acceptance letter for Article TJNPR JAN708ARN**

**Title:** *Sterculia foetida* Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: In-Vitro and *In-Silico* Study

**Authors:** Rollando Rollando\*, Warsito Warsito, Masruri Masruri, Widodo 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 full article. Our provisional acceptance of your manuscript is contingent on your responding to the Reviewers' points.

However, before the issues raised by the Reviewers are forwarded, to enable you revise your manuscript accordingly, please pay a publication charge of **\$ USD200**. The actual publication of the paper will be in the upcoming issue (Vol 5 issue 1, January 2021).

**Please state the manuscript number (TJNPR -----) 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**

TJNPR is indexed in Scopus (Elsevier) SCImago Q3 SJR 0.13

---

Editor-in-Chief: Professor Abiodun Falodun, PhD (Nigeria) Fulbright Fellow, USA  
Associate Editors: Professor Dr Peter Langer PhD Hannover (Germany)  
Professor FO Ekhaise, PhD Bayreuth (Germany)

**5. Editor mengirim hasil review artikel  
(25-12-2020)**

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

## Review Comments

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

Fri 12/25/2020 5:32 AM

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

8 attachments (20 MB)

TJNPR-2020-M387 Reviewer a.pdf; TJNPR-2020-M398 Reviewer b.pdf; TJNPR-2020-M398 Reviewer c.pdf; TJNPR-2020-M398 Reviewer d.pdf; TJNPR-2020-M398 Reviewed h.pdf; TJNPR-2020-M398 Reviewed e.docx; TJNPR-2020-M398 Reviewed f.docx; TJNPR-2020-M398 Reviewed g.docx;

Review Comments (*Sterculia foetida* Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: *In-Vitro* and *In-Silico* Study)

### Editorial comments to authors

Include date (Month and Year) of plant collection

Include the volume of Methanol used in maceration for the extraction process.

Include a section for acknowledgements if any.

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 Jan 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 (15% allowed in TJNPR) and English language editing. Evidence of the checks should be attached when submitting the revised/corrected manuscript.

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)

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Professor of Pharmaceutical Chemistry

Fellow, Fulbright (USA)

Deputy Vice-Chancellor (Academic) 2014-2016

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**A. MANUSCRIPT**

Journal	<b>Tropical Journal of Natural Product Research</b>
Manuscript Number	TJNPR JAN708AR
Type of paper	Original research
Title of paper	Sterculia foetida Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: In-Vitro and In-Silico Study
Name of Authors	

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

Abstract	In text corrections (please compare with the original manuscript)
Introduction	In text corrections (please compare with the original manuscript)
Methodology	In text corrections (please compare with the original manuscript)
Results	In text corrections (please compare with the original manuscript)
Discussion	In text corrections. (please compare with the original manuscript) I think its more ideal to pick one of the PEX9 inhibitors or a clinical approved drug as your reference compound than the sulphate ion. The lead compounds bind at residues different from GLU402 and the histidine triad as talked about in literature. Is it possible that your leads are working on other sites with allosteric activity? This might be an interesting discovery. Therefore, it is necessary to do an analysis of the binding pockets of the enzyme. Let's know which pocket each lead compound is acting on and also your standard
Conclusion	In text corrections (please compare with the original manuscript)
References	
Figures, Tables	A table is needed to show residues involved in Protein-ligand interactions for each lead compound

**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>	
<b>Short communication</b>	
Reject for reasons noted by the reviewer (please be specific)	

**E. REVIEWER'S INFORMATION**



**REVIEW FORM**

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**A. MANUSCRIPT**

Journal	<b>Tropical Journal of Natural Product Research</b>
Manuscript Number	TJNPR JAN708AR
Type of paper	Original Research
Title of paper	Sterculia foetida Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: In-Vitro and In-Silico Study
Name of Authors	<a href="mailto:ro.llando@machung.ac.id">ro.llando@machung.ac.id</a>

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

Abstract	Abstract method and resume of result explain well, but I didn't found the aim of this research
Introduction	Introduction there many active sentences, e.g., "This has led many researchers to conduct research to explore plants and chemical compounds that have cancer drugs." It should be nice to write it with passive sentences, e.g., "recent research for the plant to got chemical active compound for cancer."
Methodology	The methodology was apparent. My comment bellow <ol style="list-style-type: none"> <li>1. the first line in material and method used Bahasa, not English. Speed processor not explained well and harddisk just only 4 GB</li> <li>2. it very nice if the formula of selectivity index was explained</li> <li>3. missing character in sentence line 223 <b>Correlation of Kd values</b></li> <li>4.</li> </ol>
Results	Data of result was obvious
Discussion	About The Discussion My comment bellow <ol style="list-style-type: none"> <li>1. many active sentences,</li> <li>2. reference of selective index &lt; 2 not explained</li> <li>3. result docking its will nice if explained pharmacophore for ligand</li> </ol>
Conclusion	Conclusion was obvious
References	Conclusion was obvious
Figures, Tables	Conclusion was obvious

**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>	
<b>Short communication</b>	
Reject for reasons noted by the reviewer (please be specific)	

**E. REVIEWER'S INFORMATION**



**REVIEW FORM**

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**A. MANUSCRIPT**

Journal	<b>Tropical Journal of Natural Product Research</b>
Manuscript Number	TJNPR JAN708AR
Type of paper	Research article
Title of paper	Sterculia foetida Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: In-Vitro and In-Silico Study
Name of Authors	

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

Abstract	Abstract has included the objectives, methods, results and discussion.
Introduction	In the introduction, the research objectives have not been clearly written, it is necessary to link the background with the objectives.
Methodology	Required language improvement in software and hardware.
Results	The research results have been written in full.
Discussion	The discussion is complete
Conclusion	Conclusions have been written including all research results
References	The writing is in accordance with the guidelines.
Figures, Tables	All have been cited in manuscript.

**D. REVIEWER'S RECOMMENDATION**

Please mark with "X" one of the options.

You state the article should:

Publish as it is	X
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 JAN708AR
Type of paper	Original article
Title of paper	Sterculia foetida Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: In-Vitro and In-Silico Study
Name of Authors	

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

Abstract	The abstract is clear and comprehensive
Introduction	Introduction has explained all aspects of the research, all references are complete
Methodology	The methodology is comprehensive and includes all details of the method listed in the manuscript
Results	The research results have been explained comprehensively
Discussion	<b>It is necessary to add a correlation between molecular docking and in-vitro test results. The manuscript is not fully explained</b>
Conclusion	The conclusions made have included all the research results
References	All references have been cited in the manuscript
Figures, Tables	Figures and tables are already cited in the manuscript

**D. REVIEWER'S RECOMMENDATION**

Please mark with "X" one of the options.

You state the article should:

Publish as it is	X
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**



**6. Author mengirimkan hasil revisi artikel  
(9-1-2021)**

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

Revised article

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

Sat 1/9/2021 8:57 AM

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

 3 attachments (8 MB)

Response to reviewers.docx; Revised Article.docx; Similarity Check.pdf;

Dear Prof. Abiodun Falodun, PhD

I am herewith submitting the revised manuscript entitled "Sterculia Foetida Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: In Vitro and In Silico Study" for publication in Tropical Journal of Natural Product Research.

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

Professor Abiodun Falodun,  
Editor in Chief  
Tropical Journal of Natural Product Research

Dear Professor Abiodun Falodun,

We would like to submit our revised manuscript entitled” **Sterculia foetida Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: In-Vitro and In-Silico Study.**” for consideration of publication in the Tropical Journal of Natural Product Research.

We have response a point by point questions, comments and suggestions from the reviewer to improve our article quality as written along with this letter. We really appreciate for all these valuable comments and suggestions.

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

Thank you  
Your sincerely

Rollando, M.Sc.Apt.

## Response to Reviewers

No	Reviewer Comments	Revision
1	Please improve the writing of English.	The English writing was reviewed and corrected accordingly. All corrections were highlight in yellow.
2	Include date (Month and Year) of plant collection	The date of plant collection was stated: (March 2020)
3	Include the volume of Methanol used in maceration for the extraction process.	The volume of methanol was stated: 6 Liters.
4	Include a section for acknowledgements if any	There is no acknowledgment
5	50% of the references cited should be between 2016-2020	Reference percentage between 2016-2020 is <b>68.57%</b> , more than 50%
6	The revised and corrected manuscript should be subjected to plagiarism checker (15% allowed in TJNPR) and English language editing.	The article has been checked for plagiarism and English has been improved.
7	It is necessary to add a correlation between molecular docking and in-vitro test results. The manuscript is not fully explained	Correlation between molecular docking and in-vitro test results has been explained.
8	In general, this journal is well written. However, it needs to be revised in the background.	The background has been revised
9	I think its more ideal to pick one of the PEX9 inhibitors or a clinical approved drug as your reference compound than the sulphate ion.	I have added a PEX9 inhibitor namely NNGH. NNGH is an in vitro MMP-9 inhibitor. NNGH has an interaction energy of -5.9 kkal / mol. NNGH can interact with various amino acids in PEX-9, including GLU157 and GLN 154.
10	The lead compounds bind at residues different from GLU402 and the histidine triad as talked about in literature. Is it possible that your leads are working on other sites with allosteric activity? This might be an interesting discovery. Therefore, it is necessary to do an analysis of the binding pockets of the enzyme. Let's know which pocket each lead compound is acting on and also your standard	The results of binding pockets analysis show that the lead compounds do not interact with GLU402 and the histidine triad. This is because the lead compound acts on the other allosteric side. However, almost all compounds, sulfate ion, and positive control interact with GLU157 and GLN154.
11	A table is needed to show residues involved in Protein-ligand interactions for each lead compound	The table has been revised.
12	Abstract method and resume of result explain well, but I didn't found the aim of this research	The aim of the research has been explained.
13	Introduction there many active sentences, e.g., "This has led many researchers to conduct research to explore plants and	part of the active sentences has been revised

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

Pengajuan ke Lektor Kepala

	chemical compounds that have cancer drugs.” It should be nice to write it with passive sentences, e.g.” recent research for the plant to got chemical active compound for cancer.”	
14	the first line in material and method used Bahasa, not English. Speed processor not explained well and harddisk just only 4 GB	The sentences has been revised.
15	it very nice if the formula of selectivity index was explained	The meaning of selectivity index was explained
16	missing character in sentence line 223 Correlation of Kd values	The sentences has been revised.
17	Reference of selective index < 2 not explained	The reference was stated

***Sterculia foetida* Leaf Fraction Against Matrix Metalloproteinase-9 Protein  
and 4T1 Breast Cancer Cells: *In-Vitro* and *In-Silico* Study**

**ABSTRACT**

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***Sterculia foetida* Leaf Fraction Against Matrix Metalloproteinase-9 Protein and 4T1 Breast Cancer Cells: *In-Vitro* and *In-Silico* Studies**

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commercial, or not-for-profit sectors.

References

1. de Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *Lancet Glob Health*. 2020; 8(2):e180-90.
2. Carioli G, Malvezzi M, Bertuccio P, Hashim D, Waxman S, Negri E, et al. Cancer mortality in the elderly in 11 countries worldwide, 1970–2015. *Ann Oncol*. 2019; 30(8):1344-53.
3. Gaddam S, Heller SL, Babb JS, Gao Y. Male Breast Cancer Risk Assessment and Screening Recommendations in High-Risk Men Who Undergo Genetic Counseling and Multigene Panel Testing. *Clin Breast Cancer [Internet]*. 2020 Jul 25 [cited 2020 Nov 28]; Available from: <http://www.sciencedirect.com/science/article/pii/S1526820920301804>
4. Panieri E. Breast cancer screening in developing countries. *Best Pract Res Clin Obstet Gynaecol*. 2012; 26(2):283-90.
5. Graafland L, Abbott M, Accordini M. Breast Cancer Risk Related to Combined Oral Contraceptive Use. *J Nurse Pract*. 2020; 16(2):116-20.
6. Mondal S, Adhikari N, Banerjee S, Amin SA, Jha T. Matrix metalloproteinase-9 (MMP-9) and its inhibitors in cancer: A minireview. *Eur J Med Chem*. 2020; 194:112260.
7. Kessenbrock K, Wang C-Y, Werb Z. Matrix metalloproteinases in stem cell regulation and cancer. *Matrix Biol*. 2015; 44(46):184-90.
8. Mahomedian H, Shafiq B, Banoorahmad Awidati S, Hariono M, Ndwarga KP, Yusur M, Kouhano K, Jenie KI, Al-Najjar B. Arylamide as Potential Selective Inhibitor for Matrix Metalloproteinase 9 (MMP9): Design, Synthesis, Biological Evaluation, and Molecular Modeling. *J Chem Inf Model*. 2020; 60(1):349-59.
9. Hariono M, Rollando R, Karamoy J, Hariyono P, Atmono M, Djohan M. Bioguided Fractionation of Local Plants against Matrix Metalloproteinase9 and Its Cytotoxicity against Breast Cancer Cell Models: In Silico and In Vitro Study. *Mol Basel Switz*. 2020; 25(20).
10. Rollando R. Combination of *Hedyotis corymbosa* L. and *Tinospora crispa* ethanolic extract increase cisplatin cytotoxicity on 4T7d breast cancer cells. *Asian J Pharm Clin Res*. 2018; 171-7.
11. Cha H, Kopetzki E, Huber R, Lanzendörfer M, Brandstetter H. Structural Basis of the Adaptive Molecular Recognition by MMP9. *J Mol Biol*. 2002; 320(5):1065-79.
12. Shokoohinia Y, Gheibi S, Kiani A, Sadrajvadi K, Nowroozi A, Shahlaei M. Multi-spectroscopic and molecular modeling investigation of the interactions between prantschimgin and matrix metalloproteinase 9 (MMP9). *Lumin J Biol Chem Lumin*. 2016; 31(2):587-93.
13. Kiani A, Almasi K, Shokoohinia Y, Sadrajvadi K, Nowroozi A, Shahlaei M. Combined spectroscopy and molecular modeling studies on the binding of galbanic acid and MMP9. *Int J Biol Macromol*. 2015; 81:308-15.
14. Shakeel E, Akhtar S, Khan MKA, Lohani M, Arif JM, Siddiqui MH. Molecular docking analysis of alypsin analogs targeting survivin protein. *Bioinformation*. 2017; 13(9):293-300.
15. Dufour A, Sampson NS, Li J, Kuscic C, Rizzo RC, Deleon JL. Small-molecule anticancer compounds selectively target the hemopexin domain of matrix metalloproteinase-9. *J Biol Chem*. 2007; 282(12):8473-81.

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### Authors' Declaration

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### References

1. de Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *Lancet Glob Health*. 2020; 8(2):e180-90.
2. Carioli G, Malvezzi M, Bertuccio P, Hashim D, Waxman S, Negri E, Boffetta P, La Vecchia C. Cancer mortality in the elderly in 11 countries worldwide, 1970–2015. *Ann Oncol*. 2019; 30(8):1344-1355.
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5. Graafland L, Abbott M, Accordino M. Breast Cancer Risk Related to Combined Oral Contraceptive Use. *J Nurse Pract*. 2020; 16(2):116-20.
6. Kumbhojkar MS. Pharmacological studies on *Sterculia foetida* leaves. *Pharm Biol*. 2000; 38(1):13-7.
7. Rajasekharreddy P and Rani PU. Biofabrication of Ag nanoparticles using *Sterculia foetida* L. seed extract and their toxic potential against mosquito vectors and HeLa cancer cells. *Mater Sci Eng C Mater Biol Appl*. 2014; 39:203-12.
8. Hariono M, Nuwarda RF, Yusuf M, Rollando R, Jenie RI, Al-Najjar B. Arylamide as Potential Selective Inhibitor for Matrix Metalloproteinase 9 (MMP9): Design, Synthesis, Biological Evaluation, and Molecular Modeling. *J Chem Inf Model*. 2020; 60(1):349-59.
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10. Rollando R. Combination of *Hedyotis corymbosa* L. and *Tinospora crispa* ethanolic extract increase cisplatin cytotoxicity on t47d breast cancer cells. *Asian J Pharm Clin Res*. 2018; 171-7.
11. Cha H, Kopetzki E, Huber R, Lanzendörfer M, Brandstetter H. Structural Basis of the Adaptive Molecular Recognition by MMP9. *J Mol Biol*. 2002; 320(5):1065-79.
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**Keywords:** *Sterculia foetida*, Fraction, Cytotoxic, MMP-9, 4T1, PEX9.

Introduction

Breast cancer is one of the most common cancers in women and is the leading cause of cancer deaths worldwide.<sup>1</sup> The incidence of breast cancer increases significantly from year to year, accompanied by the tendency to be diagnosed with cancer at a young age.<sup>2</sup> The genetic heterogeneity of breast cancer in different countries is shown to be significantly different.<sup>3</sup> The incidence of breast cancer in developed countries is higher than in developing countries.<sup>4</sup> Research has shown that breast cancer's predisposing factors is known to be associated with oral contraceptive use, age, time of menopause, and ethnicity.<sup>5</sup> Besides, single nucleotide polymorphism (SNP) is a risk factor for breast cancer in individuals, although the exact mechanism of breast cancer tumorigenesis is not fully understood. Matrix metalloproteinases (MMPs) are a family of intracellularly present and zinc (Zn<sup>2+</sup>) dependent endopeptidases that can regulate other proteases, chemokines, growth factors, cytokines, and cell receptor activity.<sup>6</sup> Also, MMPs can degrade extracellular matrix components.<sup>7</sup> MMPs participate in angiogenesis, cell proliferation, immune surveillance, and apoptosis and thus play an important role in tumor initiation and development.<sup>8</sup> Specifically, Matrix metalloproteinase-9 (MMP-9) is an important member of the MMP family that plays an important role in cancer cell metastasis. The

expression of MMP-9 can change due to genetic variations that affect the effectiveness of breast cancer treatment.<sup>9</sup>

There has been many studies proving that chemical compounds in plants have cytotoxic activity. This is due to variations in the structures of the chemical compounds and the mechanisms for causing different cytotoxic effects.<sup>10</sup> This has led many researchers to conduct research to explore plants and chemical compounds that have anti-cancer effects.<sup>11</sup> *S. foetida* is a medicinal plant that has many pharmacological activities.<sup>12</sup> Mujumdar *et al.*<sup>13</sup> reported that the leaves of *S. foetida* contain luteolin,  $\alpha$ -sitosterol, scutellarein, taraxerol, n-octacosanol, and procyanidin, which have analgesic and anti-inflammatory activity. Rajasekharreddy and Rani<sup>14</sup> reported finding cyclopropene fatty acid compounds, such as (2n-octylcycloprop-1-enyl)-octanoic acid (I) from *S. foetida* seeds which have antibacterial, antiviral, and cytotoxic activities.

In this study, we explored *S. foetida* leaves fractions of n-hexane, chloroform, ethyl acetate n-butanol, and insoluble n-butanol as a possible source of compounds that have cytotoxic activities. The *in vitro* inhibitory activities of these fractions against MMP-9 protein and 4T1 cancer cells were further studied. The compounds contained in the most active fraction were identified using Gas Chromatography-Mass Spectroscopy (GC-MS). The interaction of the compounds in the most active fraction against a protein target, MMP-9 involved in cancer pathogenesis was analyzed through molecular docking techniques.

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Materials and Methods

Software and hardware

The 3D structure of PEX9 (PDBID: 1ITV), the hemopexin domain of MMP9, was downloaded from the Protein Data Bank (PDB, [www.rcsb.org](http://www.rcsb.org)), and the structures of known PEX9 inhibitors (external

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