

Journal of Ethnopharmacology

Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff. Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-hemorrhoid Herb --Manuscript Draft--

Manuscript Number:	JETHNO-D-20-01841R3
Article Type:	Research Paper
Keywords:	Graptophyllum pictum (L.) Griff, hemorrhoid, histomorphometric, croton oil, Javanese
Corresponding Author:	Katsuyoshi Matsunami Hiroshima University Hiroshima, JAPAN
First Author:	Idha Kusumawati
Order of Authors:	Idha Kusumawati Subhan Rullyansyah Rohmania . Aisyah Farah Rizka Eka Pramytha Hestianah Katsuyoshi Matsunami
Abstract:	<p>Ethnopharmacology relevance: Graptophyllum pictum (L.) Griff., known as “handeuleum” in West Java and “Daun Ungu” in Indonesia, is traditionally used to cure hemorrhoids.</p> <p>Aim of the study: The purpose of this study is to prove its effectiveness scientifically using anorectal histological parameters in Croton oil-induced hemorrhoid mice.</p> <p>Materials and methods: In vivo tests were performed by observing histomorphologic changes in mice anorectal tissue induced by croton oil. In addition, in vitro assay was performed for evaluating antioxidant activity, astringency property, and hemostasis-associated activity. The antioxidant activity was measured using a DPPH radical scavenging assay. The total flavonoid and phenolic contents were also determined spectrophotometrically.</p> <p>Results: The in vivo assay showed that the oral-topical combination use of the ethanolic extract of G. pictum leaves demonstrated significant improvement on the croton oil-induced anorectal damage better than the single application by oral or topical application.</p> <p>Conclusion: These results showed that G. pictum has potent anti hemorrhoid activity, especially for the combinational use of oral and topical administration.</p>
Suggested Reviewers:	Liva Rakotondraibe rakotondraibe.1@osu.edu Amira Wanas amira.wanas_76@yahoo.com
Response to Reviewers:	

To
Editor in Chief
Journal of Ethnopharmacology

Subject: Submission of Revised Manuscript JETHNO-D-20-01841R3

Dear Editor,

Enclosed herewith please find the revised manuscript entitled “**Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff. Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-hemorrhoid Herb**” (Idha Kusumawati, Subhan Rullyansyah, Rohmania, Aisyah Farah Rizka, Eka Pramytha Hestianah, Katsuyoshi Matsunami).

I hope that the revised manuscript is now acceptable for publication in the Journal of Ethnopharmacology.

We are looking forward to hearing your response.

Sincerely yours,

Katsuyoshi Matsunami

Professor

Department of Pharmacognosy

Graduate School of Biomedical & Health Sciences

Hiroshima University

1-2-3 Kasumi, Minami-ku, Hiroshima 734-8553, Japan;

TEL. & FAX 81-82-257-5335, e-mail: matunami@hiroshima-u.ac.jp.

Dear respectful editor and reviewers,

**Thank you for the kind and useful comments on our manuscript.
We deeply investigated the comments and then revised the manuscript
again.**

Editor and Reviewer comments:

Reviewer #1:

Thank you for answering my concerns. Although the traditional use of the plant has been appropriately referenced, the Discussion section is still a problem. It is not developed correctly. Many paragraphs are not correctly placed, and efforts to improve this section have not been appropriately conceptualized. You cannot define the mechanism/symptoms of the disease and then adapt your results. The section is not fluent, and a proper comparison to the literature is missing.

Very sorry for disturbing you again.

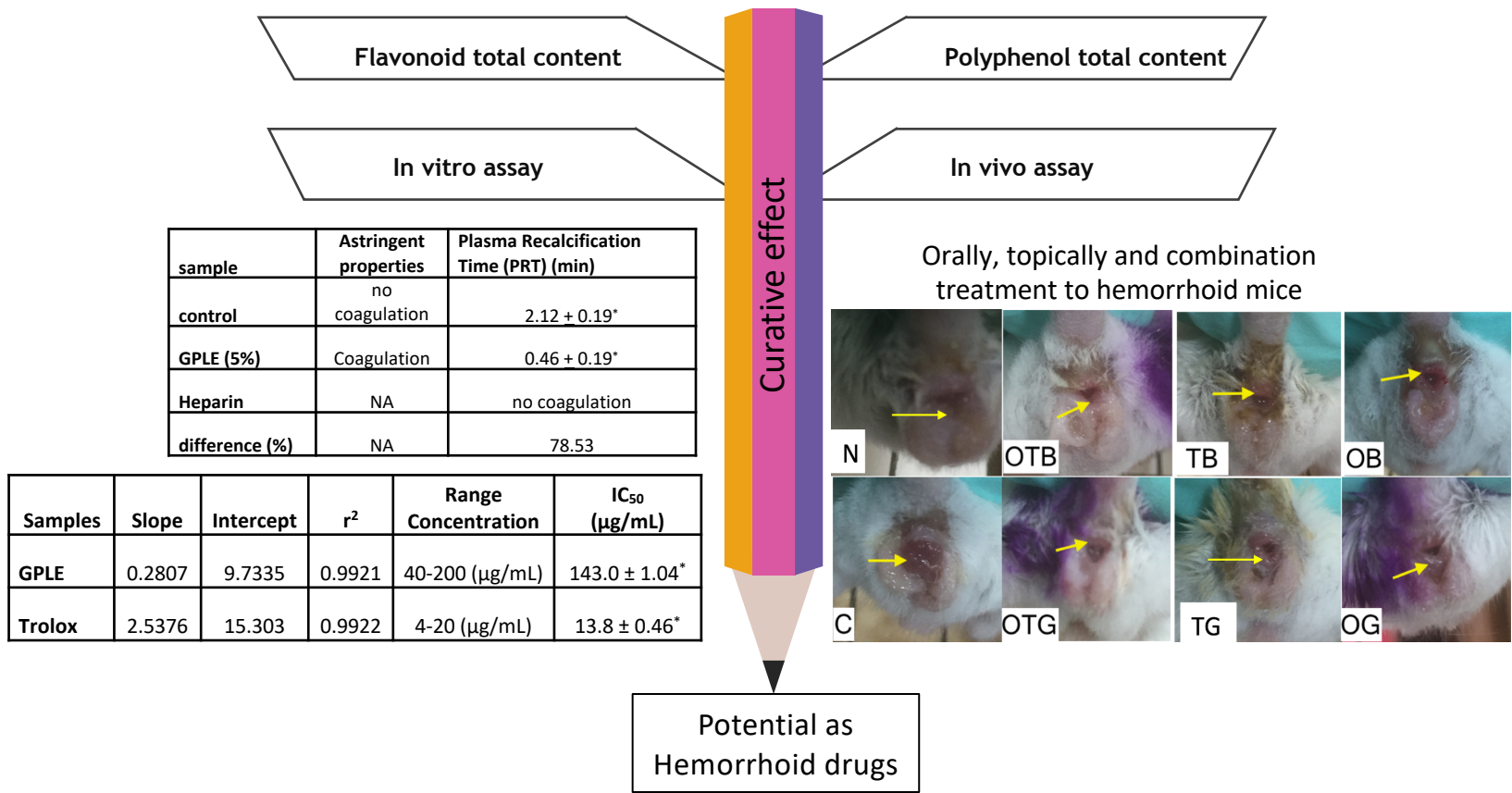
I really appreciate the important comment from the reviewer.

**The discussion section has rewrite as much as possible and we added
several reference papers according to the comment.**

I also read the main text again and corrected several minor points.

**The revised parts were highlighted in yellow. We hope this revision will
satisfy the criteria of this journal.**

Traditional uses of *G. Pictum* to cure hemorrhoid



Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Credit author statement

Conceptualization: Idha Kusumawati

Methodology: Idha Kusumawati, Rohmania, Aisyah Farah Rizka, Eka Pramyrtha Hestianah, Katsuyoshi Matsunami

Investigation: Idha Kusumawati, Subhan Rullyansyah

Resources: Idha Kusumawati, Rohmania, Aisyah Farah Rizka, Eka Pramyrtha Hestianah

Data Curation: Subhan Rullyansyah, Rohmania, Aisyah Farah Rizka, Eka Pramyrtha Hestianah

Writing - Original Draft: Idha Kusumawati, Subhan Rullyansyah

Writing - Review & Editing : Idha Kusumawati, Subhan Rullyansyah, Katsuyoshi Matsunami

Supervision: Idha Kusumawati, Katsuyoshi Matsunami

From: 松浪 勝義 matunami@hiroshima-u.ac.jp
Subject: Fw: Decision on submission to Journal of Ethnopharmacology
Date: 19 April 2021 16.44
To: idha kusumawati idha-k@ff.unair.ac.id



Dear Ms. Idha,

Please see the comments.
I'll revise them soon.

Best regards,
Katsuyoshi Matsunami, Ph.D.
Professor
Department of Pharmacognosy
Graduate School of Biomedical & Health Sciences
Hiroshima University
1-2-3, Kasumi, Minami-Ku, Hiroshima, Japan, 734-8553
E-mail: matunami@hiroshima-u.ac.jp
TEL: +81-82-257-5335

From: em.jethno.0.72bcd6.d97c6870@editorialmanager.com
<em.jethno.0.72bcd6.d97c6870@editorialmanager.com> on behalf of Journal of
Ethnopharmacology <em@editorialmanager.com>
Sent: Monday, April 19, 2021 18:36
To: 松浪 勝義 <matunami@hiroshima-u.ac.jp>
Subject: Decision on submission to Journal of Ethnopharmacology

Manuscript Number: JETHNO-D-20-01841

Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff.
Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-
hemorrhoid Herb

Dear Professor Matsunami,

Thank you for submitting your manuscript to Journal of Ethnopharmacology.

I have completed my evaluation of your manuscript. The reviewers recommend reconsideration of your manuscript following minor revision and modification. I invite you to resubmit your manuscript after addressing the comments below. Please resubmit your revised manuscript by May 19, 2021.

When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully: please outline every change made in response to their comments and provide suitable rebuttals for any comments not addressed. Please note that your revised submission may need to be re-reviewed.

To submit your revised manuscript, please log in as an author at
<https://jpn01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.editorialmanager.com%2Fjethno%2F&data=04%7C01%7Cmatunami%40hiroshima-u.ac.jp%7C377fade87d33463b694808d90316a00c%7Cc40454ddb2634926868d8e12640d3750%7C1%7C0%7C637544217971307601%7CUnknown%7CTWFPbGZsb3d8eyJWljoiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6Ik1haWwiLCJXVCi6Mn0%3D%7C1000%amp;data=VS%2F49Yb0cFkDVMop791kgeailIQBi50iKd#Kwms8CQl8%2D%2D>

<http://www.sciencedirect.com/journal/ethnopharmacology>, and navigate to the "Submissions Needing Revision" folder under the Author Main Menu.

Journal of Ethnopharmacology values your contribution and I look forward to receiving your revised manuscript.

Kind regards,

Prof.Dr. Erdem Yesilada

Associate Editor

Journal of Ethnopharmacology

Editor and Reviewer comments:

Reviewer #1: This manuscript reports the use of an extract obtained from the plant *G. pictum*. The authors partially characterized the activities of the extract. In a step forward, the authors provided an in vivo study to show the activity.

Overall, this manuscript is missing information to fulfill the 5 point of the journal.

1. There is no evidence about the traditional use of this extract. There are two references that cannot be found in the literature.
2. There is no information about the chemical profile of the extract as required for this type of study. Instead, the authors provided some general activities.

Also, the Discussion Section is poorly articulated.

Reviewer #2: The author used Ethanolic Extract of *Graptophyllum Pictum* (L.) Griff. Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Antihemorrhoid Herb, It is not new but the manuscript has important result may be give a new treatment to Hemorrhoid.

there are some notice must correct to be suitable for publication

-Dose used in the oral group, GPLE suspension was given to mice once daily with oral gavage at which concentration , must mention

- Highlight not found

- The results are expressed as means \pm SEM, must all result presented with mean \pm SD this way more statistical acceptable in the presented the result to compare between groups.

- clarify all abbreviation in the present data in tables or figures

- List the abbreviation in the same letter for ex: DPPH in 3.3. Antioxidant activity of GPLE, one mention as DPPH and in another DPPHH

- The results that presented in table 3 not suitable. Must are present the DPPH inhibition % expressed as mean \pm SD for each concentration with IC50.

- In Figure 3, 5 and 6 Hematoxylin and eosin staining of histological sections of hemorrhoid anorectal from croton oil-induced, add a picture in high magnification to give more details and clarity in histopathological changing.

For further assistance, please visit our customer service site:

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<https://jpn01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.editorialmanager.com%2Fjethno%2Flogin.asp%3Fa%3Dr&data=04%7C01%7Cmatunami%40hiroshima-u.ac.jp%7C377fade87d33463b694808d90316a00c%7Cc40454ddb2634926868d8e12640d3750%7C1%7C0%7C637544217971317599%7CUnknown%7CTWFpbGZsb3d8eyJWlloiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C1000&data=wVbV7AEDjxryQ5crYyTIOnwHIFytCbqA7rUj%2BbzeeLY%3D&reserved=0>). Please contact the publication office if you have any questions.



JETHNO-
D-20-01841.pdf

From: Idha Kusumawati idha-k@ff.unair.ac.id 
Subject: Re: Decision on submission to Journal of Ethnopharmacology
Date: 4 May 2021 06.06
To: 松浪 勝義 matunami@hiroshima-u.ac.jp

IK

Dear Matsunami Sensei,

I have revised the article, and I also make the answer of the comment from the reviewer. Please check.
Thank you



The answer to
Reviewer.docx



draft
030521.docx

Best regards,
Idha Kusumawati
Department of Pharmaceutical Science
Faculty of Pharmacy, Airlangga University
Surabaya-Indonesia

On 19 Apr 2021, at 16.44, 松浪 勝義 <matunami@hiroshima-u.ac.jp> wrote:

Dear Ms. Idha,

Please see the comments.
I'll revise them soon.

Best regards,
Katsuyoshi Matsunami, Ph.D.
Professor
Department of Pharmacognosy
Graduate School of Biomedical & Health Sciences
Hiroshima University
1-2-3, Kasumi, Minami-Ku, Hiroshima, Japan, 734-8553
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TEL: +81-82-257-5335

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on behalf of Journal of Ethnopharmacology <em@editorialmanager.com>
Sent: Monday, April 19, 2021 18:36
To: 松浪 勝義 <matunami@hiroshima-u.ac.jp>
Subject: Decision on submission to Journal of Ethnopharmacology

Manuscript Number: JETHNO-D-20-01841

Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff. Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-hemorrhoid Herb

Dear Professor Matsunami,

Thank you for submitting your manuscript to Journal of Ethnopharmacology.

I have completed my evaluation of your manuscript. The reviewers recommend reconsideration of your manuscript following minor revision and modification. I invite you to resubmit your manuscript after addressing the comments below. Please resubmit your revised manuscript by May 19, 2021.

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To submit your revised manuscript, please log in as an author at <https://jpn01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.editorialmanager.com%2Fjethno%2F&data=04%7C01%7Cmatunami%40hiroshima-u.ac.jp%7C377fade87d33463b694808d90316a00c%7Cc40454ddb2634926868d8e12640d3750%7C1%7C0%7C637544217971307601%7CUnknown%7CTWFpbGZsb3d8eyJWlloiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBbTl6lk1haWwiLCJXVCi6Mn0%3D%7C1000&data=VS%2B48Xb0eEkPIVcn73UxgggjUOBi50iKdfKgwp8GOL8%3D&reserved=0>, and navigate to the "Submissions Needing Revision" folder under the Author Main Menu.

Journal of Ethnopharmacology values your contribution and I look forward to receiving your revised manuscript.

Reviewer #1: This manuscript reports the use of an extract obtained from the plant *G. pictum*. The authors partially characterized the activities of the extract. In a step forward, the authors provided an in vivo study to show the activity.

Overall, this manuscript is missing information to fulfill the 5 point of the journal.

Here is the 5 point of the journal:

1. Out of scope
The paper should report on traditional use or present results on pharmacological or toxicological studies (positive or negative) that are directly related to the traditional use. These data should eventually contribute to evidence-based traditional medicines.
2. Too preliminary
A paper must be based on a thorough and extensive study, using proper controls.
3. In-vitro antioxidant activity
Antioxidant activity is present in all plants. Screening with in-vitro assays thus has little meaning if no clear evidence is given for in-vivo activity.
4. Ethnopharmacological and ethnobotanical surveys normally need to report primary (absolute) data reporting how many times a (botanical) drug has been cited for a certain use and application.
Authors must comply with all relevant standards in the field.
5. Lack of novelty
The study must represent a novel approach to the study of the activity, i.e. not more or less repeating what has already been published with similar results, but e.g. only using another extract of the same plant, or, in case of antimicrobial activity, some other microorganisms.

All of these point is fulfilled in our article.

1. There is no evidence about the traditional use of this extract. There are two references that cannot be found in the literature.

There is a lot of information about ethnomedicine or the traditional use of this plant for hemorrhoid therapy in Indonesia. Still, the existing literature is Indonesian and not international, so it isn't easy to find. The two pieces of literature cited in this article is also old textbooks that are very well known by Heyne K from the Dutch colonial era in Indonesia. This literature means that it is accurate ethnomedicine data.

- A. Heyne, K., 1987. *Tumbuhan Berguna Indonesia Volume 3*. Yayasan Sarana Wana Jaya, Jakarta.
- B. Levang, P., Foresta, H. de, 1991. *Economic plants of Indonesia: a Latin, Indonesian, French and English dictionary of 728 species*, Orstom and SEAMEO BIOTROP. ORSTOM and SEAMEO BIOTROP.
- C. Ministry of Health, R.I., 2010. *Guidelines for The Use of Herbal Medicines in Family Health Care*. Ministry of Health.
- D. Ramdhan, B., Chikmawati, T., Waluyo, E.B., 2015. *Ethnomedical Herb from Cikondang Indigenous Village, District Bandung*. *J. Biodivers. Environ. Sci. J. Bio. Env. Sci* 6, 277–288

2. There is no information about the chemical profile of the extract as required for this type of study. Instead, the authors provided some general activities.

Information regarding chemical profiles has been done before (other chemical substances such as myricetin and kaempferol (Kusumawati et al., 2002)) especially on flavonoid compounds according to the Ozaki (Ozaki, Y., Sekita, S., Soedigdo, S., Harada, M., 1989. Antiinflammatory Effect of *Graptophyllum pictum* (L.) Griff. Chem. Pharm. Bull. 37, 2799–2802.)

Also, the Discussion Section is poorly articulated.

Thanks for the correction. We have revised the discussion section.

Reviewer #2: The author used Ethanolic Extract of *Graptophyllum Pictum* (L.) Griff. Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Antihemorrhoid Herb, It is not new but the manuscript has important result may be give a new treatment to Hemorrhoid. there are some notice must correct to be suitable for publication

-Dose used in the oral group, GPLE suspension was given to mice once daily with oral gavage at which concentration , must mention

The oral dosage per day is listed in table 1

- Highlight not found

Thanks for the correction. Here we add the highlight.

Highlights:

- *Graptophyllum pictum* (L.) Griff. are traditionally used to cure hemorrhoid in Indonesia
- Symptoms of hemorrhoid include bleeding, pain, prolapsing, swelling, itching, and mucus soiling
- Astringent activity and Plasma recalcification time is an important factor in hemostasis
- *Graptophyllum pictum* leaves exhibited a healing process on hemorrhoids through anti-inflammatory, hemostasis and antioxidant properties
- The oral-topical combination administration of GPLE (OTG) would effectively treat hemorrhoidal pathological conditions.

- The results are expressed as means \pm SEM, must all result presented with mean \pm SD this way more statistical acceptable in the presented the result to compare between groups.

Thanks for the correction. We've revised it to \pm SD.

- clarify all abbreviation in the present data in tables or figures

Thanks for the correction. We've added the abbreviation to all figures and tables.

- List the abbreviation in the same letter for ex: DPPH in 3.3. Antioxidant activity of GPL, one mention as DPPH and in another DPPHH

Thanks for the correction. We've revised it.

- The results that presented in table 3 not suitable. Must are present the DPPH inhibition % expressed as mean \pm SD for each concentration with IC50.

DPPH inhibition% data is presented in Figure 1. The data in Table 3 shows the IC50 of the sample (GPL) and Trolox (standart) derived from the data in Figure 1.

- In Figure 3, 5 and 6 Hematoxylin and eosin staining of histological sections of hemorrhoid anorectal from croton oil-induced, add a picture in high magnification to give more details and clarity in histopathological changing.

Fig.3 with a magnification of 200x, it can show the difference between the control group and the normal group. The induction of croton oil causes an increase in thickness of M, MEL, and MES and an increase in the number of inflammatory cells in MES.

Fig.5. Only shows what parameters are measured on the mucosa not to show any changes after treatment.

Fig.6. Only shows what parameters are measured on the muscularis externa not to show any changes after treatment.

The changes after treatment are shown in Fig. 4 and Tables 4 and 5

From: 松浪 勝義 matunami@hiroshima-u.ac.jp
Subject: Re: Decision on submission to Journal of Ethnopharmacology
Date: 5 May 2021 07.45
To: idha kusumawati idha-k@ff.unair.ac.id



Dear Dr. Idha,

Thank you for the comments.
I'll reply to the editor after checking it.

Best regards,
Katsuyoshi Matsunami, Ph.D.
Professor
Department of Pharmacognosy
Graduate School of Biomedical & Health Sciences
Hiroshima University
1-2-3, Kasumi, Minami-Ku, Hiroshima, Japan, 734-8553
E-mail: matunami@hiroshima-u.ac.jp
TEL: +81-82-257-5335

From: idha kusumawati <idha-k@ff.unair.ac.id>
Sent: Tuesday, May 4, 2021 8:05
To: 松浪 勝義 <matunami@hiroshima-u.ac.jp>
Subject: Re: Decision on submission to Journal of Ethnopharmacology

Dear Matsunami Sensei,

I have revised the article, and I also make the answer of the comment from the reviewer. Please check.
Thank you

Best regards,
Idha Kusumawati
Department of Pharmaceutical Science
Faculty of Pharmacy, Airlangga University
Surabaya-Indonesia

On 19 Apr 2021, at 16.44, 松浪 勝義 <matunami@hiroshima-u.ac.jp> wrote:

Dear Ms. Idha,

Please see the comments.
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Best regards,
Katsuyoshi Matsunami, Ph.D.
Professor
Department of Pharmacognosy
Graduate School of Biomedical & Health Sciences
Hiroshima University
1-2-3, Kasumi, Minami-Ku, Hiroshima, Japan, 734-8553
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When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully: please outline every change made in response to their comments and provide suitable rebuttals for any comments not addressed

From: 松浪 勝義 matunami@hiroshima-u.ac.jp
Subject: Fw: Decision on submission to Journal of Ethnopharmacology
Date: 26 July 2021 07.42
To: idha kusumawati idha-k@ff.unair.ac.id



Dear Dr. Idha,

We received minor revision again.
But it's not so serious.
Could you revise again according to the comments below.

Best regards,
Katsuyoshi Matsunami, Ph.D.
Professor
Department of Pharmacognosy
Graduate School of Biomedical & Health Sciences
Hiroshima University
1-2-3, Kasumi, Minami-Ku, Hiroshima, Japan, 734-8553
E-mail: matunami@hiroshima-u.ac.jp
TEL: +81-82-257-5335

From: em.jethno.0.74df9d.64e850c5@editorialmanager.com
<em.jethno.0.74df9d.64e850c5@editorialmanager.com> on behalf of Journal of
Ethnopharmacology <em@editorialmanager.com>
Sent: Sunday, July 25, 2021 23:30
To: 松浪 勝義 <matunami@hiroshima-u.ac.jp>
Subject: Decision on submission to Journal of Ethnopharmacology

Manuscript Number: JETHNO-D-20-01841R1

Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff.
Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-
hemorrhoid Herb

Dear Professor Matsunami,

Thank you for submitting your manuscript to Journal of Ethnopharmacology.

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To submit your revised manuscript, please log in as an author at
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[eyJWljoimC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6Ik1haWwiLCJXVCi6Mn0%3D%7C1000&reserved=0](https://jpn01.safelinks.protection.outlook.com/?url=http%3A%2F%2Fwww.elsevier.com%2Fdib-template&data=04%7C01%7Cmatunami%40hiroshima-u.ac.jp%7Ceed02803e86f4ce2ce2308d94f78d0b9%7Cc40454ddb2634926868d8e12640d3750%7C1%7C0%7C637628202579578578%7CUnknown%7CTWFpbGZsb3d8eyJWljoimC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6Ik1haWwiLCJXVCi6Mn0%3D%7C1000&reserved=0), and navigate to the "Submissions Needing Revision" folder under the Author Main Menu.

Journal of Ethnopharmacology values your contribution and I look forward to receiving your revised manuscript.

Kind regards,

Erdem Yesilada

Associate Editor

Journal of Ethnopharmacology

Editor and Reviewer comments:

The authors have partially answered my concerns. Regarding the ethnopharmacological use, I suggest to add a copy of the paragraph where the use is mentioned and translate to English. This information can be uploaded as a Supplementary Information with reference in the main text. The Discussion section has not been improved, it looks that patches with repetition of the results or background. This section is still to be developed.


Data in Brief (optional):

We invite you to convert your supplementary data (or a part of it) into an additional journal publication in Data in Brief, a multi-disciplinary open access journal. Data in Brief articles are a fantastic way to describe supplementary data and associated metadata, or full raw datasets deposited in an external repository, which are otherwise unnoticed. A Data in Brief article (which will be reviewed, formatted, indexed, and given a DOI) will make your data easier to find, reproduce, and cite.

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From: idha kusumawati idha-k@ff.unair.ac.id 
Subject: Re: Decision on submission to Journal of Ethnopharmacology
Date: 11 August 2021 17.18
To: 松浪 勝義 matunami@hiroshima-u.ac.jp

IK

Dear Matsunami Sensei,

I have revised the Discussion section.
I also attach the copy of the reference below.
I hope it is in accordance with the reviewer's request.



draft
100821.docx



translated
reference.docx



Heyne.pdf



MINISTRY OF
HEALT...10.pdf

Best regards,
Dr. Idha Kusumawati

On 26 Jul 2021, at 07.42, 松浪 勝義 <matunami@hiroshima-u.ac.jp> wrote:

Dear Dr. Idha,

We received minor revision again.
But it's not so serious.
Could you revise again according to the comments below.

Best regards,
Katsuyoshi Matsunami, Ph.D.
Professor
Department of Pharmacognosy
Graduate School of Biomedical & Health Sciences
Hiroshima University
1-2-3, Kasumi, Minami-Ku, Hiroshima, Japan, 734-8553
E-mail: matunami@hiroshima-u.ac.jp
TEL: +81-82-257-5335

From: em.jethno.0.74df9d.64e850c5@editorialmanager.com <em.jethno.0.74df9d.64e850c5@editorialmanager.com>
on behalf of Journal of Ethnopharmacology <em@editorialmanager.com>

Sent: Sunday, July 25, 2021 23:30

To: 松浪 勝義 <matunami@hiroshima-u.ac.jp>

Subject: Decision on submission to Journal of Ethnopharmacology

Manuscript Number: JETHNO-D-20-01841R1

Histomorphometric Study of Ethanollic Extract of Graptophyllum Pictum (L.) Griff. Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-hemorrhoid Herb

Dear Professor Matsunami,

Thank you for submitting your manuscript to Journal of Ethnopharmacology.

I have completed my evaluation of your manuscript. The reviewers recommend reconsideration of your manuscript following minor revision and modification. I invite you to resubmit your manuscript after addressing the comments below. Please resubmit your revised manuscript by Aug 24, 2021.

When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully: please outline every change made in response to their comments and provide suitable rebuttals for any comments not

Heyne, K., 1987. Tumbuhan Berguna Indonesia Volume 3. Yayasan Sarana Wana Jaya, Jakarta

Demikian pula di Jawa daun ini mempunyai reputasi yang besar sebagai obat untuk menyembuhkan bengkak-bengkak dan bisul. Ny. Kloppenburg mengatakan bahwa air seduhan daun wungu yang dimaksud bukanlah *Lagerstromia speciosa* melainkan *Graptophyllum pictum*, dicampur dengan daun urat (*Plantago Mayor*), dalam penggunaan secara terus-menerus dapat menyembuhkan bawazir, dan bunganya diminum seperti the (obat signatur) berguna untuk melancarkan menstruasi.

English translate:

Likewise, this leaf has an excellent reputation as a medicine to cure swellings and ulcers in Java. Mrs. Kloppenburg said that the brewed water of Daun wungu (was not *Lagerstromia speciosa* but *Graptophyllum pictum*), mixed with *Plantago Mayor*, can cure hemorrhoids in continuous use and the tea of the flowers (signature medicine), which is useful for menstrual disorders.

Ministry of Health, R.I., 2010. Guidelines for The Use of Herbal Medicines in Family Health Care 115.

Graptophyllum pictum [L.] Griff.

Family : Acanthaceae
Indonesian name : daun ungu
English name : caricature plant
Other name : san tse che (Chinese)
Chemical constituents : alkaloid, glycoside, steroid, saponin, tannin, calciumoxalate
Part of plant used : leaf, flower, bark
Use : haemorrhoid, bruise, skin ulcer, constipation
Plant propagation : stem cutting

akhir *A. volubilis* WALL. Kedua macam tanaman ini disatukan oleh Linnaeus menjadi *A. ilicifolius*, yang oleh kebanyakan ahli tumbuh-tumbuhan ditetapkan sebagai jenis.

***Andrographis paniculata* NEES.**

Nama daerah *Creat* - Ind.: *Pépaitan* (Mal.) - Sund.: *Ki Oray, Ki peurat, Takilo* - Jaw.: *Bidara, Sadilata, Sambilata, Takila*.

Terna, tumbuh lurus, bercabang banyak, tinggi 0,50 hingga 0,80 m, sejak dahulu kala oleh orang Jawa dianggap sebagai obat mujarab terhadap gigitan ular berbisa: orang yang digigit ular memasukkan sedikit tanaman itu ke mulutnya, mengunyahnya beberapa lama, kemudian menelan air ludahnya dan ampas kunyahan itu diletakkan pada luka. (Boorsma: *Plantenstoffen* II, hlm. 63 dan III, hlm. 59). Dalam het *Geneesk. Tijdschr. v. N.I.* 1908, hlm. 657, ia memberitahukan bahwa *sadilata* mungkin sekali tidak berbahaya, ia mempunyai juga suatu reputasi sebagai obat untuk menyembuhkan penyakit gula dan menganjurkan untuk menggunakannya terhadap penyakit lain yang masih banyak lagi. Ny. Kloppenburg menyebutkan, bahwa selain untuk mengobati gigitan dari serangga yang berbisa dan merusak, juga bila dicampur dengan daun *kumis kucing* (*Orthosiphon*) dapat mengobati penyakit gula (*diabetis*), air perasan daun dapat digunakan sebagai obat kompres bila demam dan bila air perasan dari daun yang ditumbuk itu disaring kemudian diminum dapat menyembuhkan penyakit typhus dan demam, akan tetapi harus berhati-hati melakukannya karena dapat mengakibatkan mata menjadi bengkak. Selanjutnya Dr. Boorsma memberitahukan kepada penulis, bahwa daun-daun yang ditumbuk ternyata baik kerjanya dalam beberapa hal mengenai penyakit-penyakit kulit yang gatal, yang dengan obat lain tidak dapat disembuhkan, dan air seduhan atau pil yang berasal dari daun-daun tersebut sangat dianjurkan sebagai obat penyakit perempuan. Penelitian kimia yang dilakukannya memperlihatkan adanya suatu kesenyawaan alkalis yang dapat menguap, walaupun demikian dalam prakteknya ia tidak menimbulkan keracunan yang berarti. Selanjutnya dari suatu bahan pahit yang telah diteliti oleh Gorter (*Recueil des Trav. Chim.* XXX, hlm. 152), yang belum diuji, apakah ia barangkali harus dianggap suatu komponen aktif, padahal memang nyata, bahwa ia tidak sangat beracun. Di sini terdapat juga kadar kalium yang tinggi: dalam 15,9 gram terna kering udara terdapat 417 mgr. kalium dan hanya 26 mgr. natrium.

Kimia

***Asystasia intrusa* BL. (A. Blumei NEES).**

Nama daerah. Mel. Mal.: *Daun moreto, Cili hutan* - Halmah. Sel.: *Luja koi* (Weda) - Halmah. Ut.: *Luja madorau* (Gal., Tob.).

Menurut *uraian* Rumphius (VI, hlm. 53), *Moretiana* yang tidak cocok dengan ujudnya, ialah suatu terna yang tumbuh berbaring dengan batangnya yang hampir sebesar batang padi, cenderung tumbuh di muara-muara sungai di bawah belukar. Seluruh bagian tanaman ini digiling dengan bawang dan air *lemon swangi* menghasilkan cairan yang dapat digunakan terhadap batuk kering dan sekaligus terhadap gatal-gatal di tenggorokan dan sesak pada pernapasan. Air perasan daun yang berbau air got itu ditetaskan kepada mata yang merah, sehingga mata tersebut menjadi sejuk, bersih dan jernih (R.).

***Graptophyllum pictum* GRIFF (G. hortense NEES.).**

Nama daerah *Germantine peinte, Gertenschriftblatt, Carricature plant* - Simalur: *Pudin* (Tapan) - Mel.: *Dangora* (Mal.): *Daun putri* (Amb.), *Puding, puding perada* - Sund.: *Daun ungu, D. tēmēn-tēmēn, Handeu-*

leum - Jaw.: *Dēmung, Tulak, Wungu* - Mad.: *Karoton, Karotong* - Bal.: *Tēmēn* - Ternate: *Kabi-kabi* - Tidore: *Dongo-dongo*.

Perdu yang tumbuh lurus, tinggi 1½ hingga 8 m, mungkin sekali berasal dari Irian Jaya; di Jawa tumbuh dari dataran rendah hingga pada ketinggian kurang lebih 1250 m di atas permukaan laut, sering ditanam sebagai tanaman hias atau tanaman pagar; varietas yang berdaun merah itu sebagaimana halnya dengan *Cordyline fruticosa* BACKER banyak sekali digunakan sebagai tanda batas di kebun-kebun teh. Tanaman ini mudah sekali diperbanyak dengan menggunakan stek (Backer). Rumphius (IV, hlm. 73) menguraikan beberapa forma dengan nama *Folium bracteatum* dan memberitahukan pemakaiannya, sebagai berikut. Kulit dan daunnya terasa seperti lendir dan berbau busuk; yang pertama, kulit tanaman ditumbuk dan diletakkan pada berbagai macam bengkak baru, dapat melenyapkan bengkak itu. Juga daun-daunnya dilayukan dan diperam supaya masak. Daun dari forma balang-balang merah oleh perempuan-perempuan Ternate sangat dihargai sebagai obat untuk menyembuhkan bisul di dada: daun itu lebih dahulu diolesi santan kelapa lalu dipanaskan di atas api, kemudian diletakkan di tempat yang sakit. Daun-daun dari forma merah setelah digiling hingga menjadi bubur, dipandang lebih cocok untuk mematangkan bengkak dan bisul yang panas (R.). Demikian pula di Jawa daun ini mempunyai reputasi yang besar sebagai obat untuk menyembuhkan bengkak-bengkak dan bisul. Ny. Kloppenburg mengatakan, bahwa air seduhan *daun wungu* yang dimaksud bukanlah *Lagerstroemia speciosa*, melainkan *Graptophyllum pictum*, dicampur dengan *daun urat* (*Plantago*), dalam penggunaan secara terus-menerus dapat menyembuhkan bawazir, dan bunganya diminum seperti teh (obat signatur) berguna untuk melancarkan menstruasi. Bahan-bahan organik yang dapat diharapkan mengandung suatu khasiat yang khusus tidak ditemukan penelitian yang dilakukan oleh Boorsma (*Plantenstoffen II*, hlm. 47).

Kulit

Daun

Bunga

***Pseuderanthemum diversifolium* MIQ.** (*Erapthemum* d. MIQ.).
Nama daerah. Jaw.: *Posor*.

Terna, tumbuh tegak, dengan ketinggian 0,50 hingga 0,80 m. Ny. Kloppenburg ketika menggambarkannya memberi nama *Graptophyllum hortense*, memberitahukan bahwa daun posor yang digiling bersama *bunga lawang* (*Cinnamomum*) ditapelkan di bawah perut, bila sukar buang air kecil.

***Pseuderanthemum racemosum* RADLK.**
nama daerah. Mel. Mal.: *Sayur kambing*.

Rumphius menguraikan *Olus caprinum* (VI, hlm. 54) sebagai suatu terna yang 2½ kaki tingginya muncul dengan satu batang, lebih suka tumbuh di bawah pohon-pohon kelapa dan di tempat-tempat teduh lainnya yang agak lembab. Kambing suka sekali memakannya dan juga sangat baik untuk sayur (R.).

***Peristrophe bivalvis* MERR.** (*P. tinctoria* NEES.).

Nama daerah. Aceh: *Mujèë, Ojè* - Gayo: *Rajang* - Simalur: *Anusa* - Mel.: *Anajo, Ananjo, Daun benang* (Mal.), *Indujau, Najo, Noja, Ujai* (Bangka) - Jawa: *Noja* - Alf. Sul. Ut.: *Kololuda* (mongond.), *Lëlënu* (t.t.) - Boul: *Anudoh* - Barea: *Andudu* - Mak.: *Anruda* - Bug.: *Amuja*.

Terna, menyerupai perdu, tersebar di seluruh Nusantara dan di mana-mana digunakan untuk memberi warna merah bagi bahan-bahan anyaman. Rumphius



Guidelines for The Use of Herbal Medicines in Family Health Care



MINISTRY OF HEALTH
REPUBLIC OF INDONESIA
2010



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Guidelines for The Use of Herbal Medicines in Family Health Care

Sixth Edition

MINISTRY OF HEALTH
REPUBLIC OF INDONESIA
2010



615.323 Indonesia Ministry of Health
Ind Directorate General of Public Health
P Directorate of Community Participation

Ministry of Health, 1991

- I. Title
 - 1. Medicinal Plants
 - 2. Family Health





FIRST EDITION

1st PRINT : YEAR 1991

2ND PRINT : YEAR 1992

SECOND EDITION

3RD PRINT : YEAR 1993

THIRD EDITION

4TH PRINT : YEAR 1995/1996

5TH PRINT : YEAR 1996/1997

6TH PRINT : YEAR 1998/1999

7TH PRINT : YEAR 1999

FOURTH EDITION

8TH : YEAR 2000

9TH : YEAR 2001

FIFTH EDITION

10TH : YEAR 2004

SIXTH EDITION

11TH PRINT : YEAR 2009

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REMEDIES FROM MEDICINAL PLANTS IN THIS BOOK ARE SELECTED MEDICINAL PLANTS OR HERBS BASED ON RECIPES FROM VARIOUS INDONESIAN COMMUNITIES, BEING USED FOR MORE THAN THREE GENERATIONS. THESE PLANTS WERE SELECTED AND HAVE EVIDENCE BASED ON THE PRE-CLINICAL STUDIES, TOXICITY STUDIES AND PHARMACODYNAMIC STUDIES.

THEREFORE, THEY ARE CONSIDERED TO BE SAFE AND BENEFICIAL TO OVERCOME AILMENTS IN THE FAMILY.





***Graptophyllum pictum* [L.] Griff.**

Family	: Acanthaceae
Indonesian name	: daun ungu
English name	: caricature plant
Other name	: san tse che (Chinese)
Chemical constituents	: alkaloid, glycoside, steroid, saponin, tannin, calcium oxalate
Part of plant used	: leaf, flower, bark
Use	: haemorrhoid, bruise, skin ulcer, constipation
Plant propagation	: stem cutting



***Gynura segetum* (Lour.) Merr.**

Family	: Asteraceae
Indonesian name	: daun dewa
English name	: -
Other name	: samsit
Chemical constituents	: alkaloid, saponin, flavonoids, volatile oil, tannin
Part of plant used	: whole plant and bulb
Use	: burn wound, skin ulcer, bruised skin, snake bite
Plant propagation	: bulb, stem cutting

From: 松浪 勝義 matunami@hiroshima-u.ac.jp
Subject: Fw: Decision on submission to Journal of Ethnopharmacology
Date: 30 August 2021 07:52
To: idha kusumawati idha-k@ff.unair.ac.id



Dear Dr. Idha,

The reviewer still has some concern on the discussion.
Please try to improve it.

Best regards
Katsuyoshi Matsunami, Ph.D.
Professor
Department of Pharmacognosy
Graduate School of Biomedical & Health Sciences
Hiroshima University
1-2-3, Kasumi, Minami-Ku, Hiroshima, Japan, 734-8553
E-mail: matunami@hiroshima-u.ac.jp
TEL: +81-82-257-5335

From: em.jethno.0.75994c.7868de60@editorialmanager.com
<em.jethno.0.75994c.7868de60@editorialmanager.com> on behalf of Journal of
Ethnopharmacology <em@editorialmanager.com>
Sent: Friday, August 27, 2021 23:46
To: 松浪 勝義 <matunami@hiroshima-u.ac.jp>
Subject: Decision on submission to Journal of Ethnopharmacology

Manuscript Number: JETHNO-D-20-01841R2

Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff.
Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-
hemorrhoid Herb


Dear Professor Matsunami,

Thank you for submitting your manuscript to Journal of Ethnopharmacology.

I have completed my evaluation of your manuscript. The reviewers recommend reconsideration of your manuscript following minor revision and modification. I invite you to resubmit your manuscript after addressing the comments below. Please resubmit your revised manuscript by Sep 10, 2021.

When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully: please outline every change made in response to their comments and provide suitable rebuttals for any comments not addressed. Please note that your revised submission may need to be re-reviewed.

To submit your revised manuscript, please log in as an author at
<https://jpn01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.editorialmanager.com%2Fjethno%2F&data=04%7C01%7Cmatunami%40hiroshima-u.ac.jp%7Ceb3258f72f834868943108d969696f4b%7Cc40454ddb2634926868d8e12640d3750%7C1%7C1%7C637656723824747579%7CUnknown%7CTWFpbGZsb3d8eYJWljoicMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTil6lk1haWwiLCJXVCi6Mn0%3D%7C2000%20amp%20date%20%3A%2F%2F2021%2F08%2F30%2007%3A52%3A00%3A00>

From: idha kusumawati idha-k@ff.unair.ac.id 
Subject: Re: Revision of "Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff. Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-hemorrhoid Herb" is due soon
Date: 3 September 2021 16.41
To: 松浪 勝義 matunami@hiroshima-u.ac.jp

IK

Dear Matsunami Sensei,

I have send the revised article on August 31.
Herewith I send it again.



draft
300821.docx

Best regards,

Dr. Idha Kusumawati
Department of Pharmaceutical Science
Faculty of Pharmacy, Airlangga University

On 3 Sep 2021, at 15.51, 松浪 勝義 <matunami@hiroshima-u.ac.jp> wrote:

Dear Dr. Idha,

The due date is Sep 10.
Sorry for your effort.

Best regards,
Katsuyoshi Matsunami, Ph.D.
Professor
Department of Pharmacognosy
Graduate School of Biomedical & Health Sciences
Hiroshima University
1-2-3, Kasumi, Minami-Ku, Hiroshima, Japan, 734-8553
E-mail: matunami@hiroshima-u.ac.jp
TEL: +81-82-257-5335

From: em.jethno.5289.75bef2.e6955d0b@editorialmanager.com <em.jethno.5289.75bef2.e6955d0b@editorialmanager.com> on behalf of Erdem Yesilada <em@editorialmanager.com>
Sent: Friday, September 3, 2021 16:23
To: 松浪 勝義 <matunami@hiroshima-u.ac.jp>
Subject: Revision of "Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff. Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-hemorrhoid Herb" is due soon

This is an automated message.

Manuscript Number: JETHNO-D-20-01841R2
Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff. Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-hemorrhoid Herb

Dear Professor Matsunami,

We would like to remind you that on Aug 27, 2021 we asked you to revise your above referenced manuscript and your revision is due by Sep 10, 2021.

Journal of Ethnopharmacology values your contribution and we look forward to receiving your revised manuscript.

To submit your revision, please log in as an author at <https://jpn01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.editorialmanager.com%2FJETHNO%2F&data=04%7C01%7Cmatunami%40hiroshima-u.ac.jp%7C9b6737ef13744dde5c2508d96eabca09%7Cc40454ddb2634926868d8e12640d3750%7C1%7C1%7C637662506377250545%7CUnknown%7CTWFPbGZsb3d8eyJWljojoiMC4wLjAwMDAilLCJQljojoiV2luMzliLlCJBTiI6IklhaWwiLlCJXVCi6Mn0%3D%7C3000&data=fffQ3RJsmaMCKfegTDRLIfhO63ohSYnBI8enOdHu%2Bt4%3D&reserved=0>, and navigate to the "Submissions Needing Revision" folder under the Author Main Menu. You will also find the decision letter and comments available there.

If you do not plan to revise your manuscript, please click "Decline to Revise" in the "Submissions Needing Revision" folder.

If you require more time, please contact the journal office by replying to this email.

Kind regards,
Journal of Ethnopharmacology

From: 松浪 勝義 matunami@hiroshima-u.ac.jp
Subject: Fw: Decision on submission to Journal of Ethnopharmacology
Date: 19 October 2021 15.55
To: idha kusumawati idha-k@ff.unair.ac.id



Dear Dr. Idha,

Thank you for your kind collaboration.
We have received the acceptance.

Best regards,
Katsuyoshi Matsunami, Ph.D.
Professor
Department of Pharmacognosy
Graduate School of Biomedical & Health Sciences
Hiroshima University
1-2-3, Kasumi, Minami-Ku, Hiroshima, Japan, 734-8553
E-mail: matunami@hiroshima-u.ac.jp
TEL: +81-82-257-5335

From: em.jethno.0.76c17e.811f8438@editorialmanager.com
<em.jethno.0.76c17e.811f8438@editorialmanager.com> on behalf of Journal of
Ethnopharmacology <em@editorialmanager.com>
Sent: Tuesday, October 19, 2021 15:31
To: 松浪 勝義 <matunami@hiroshima-u.ac.jp>
Subject: Decision on submission to Journal of Ethnopharmacology

Manuscript Number: JETHNO-D-20-01841R3

Histomorphometric Study of Ethanolic Extract of Graptophyllum Pictum (L.) Griff.
Leaves on Croton Oil-Induced Hemorrhoid Mice: A Javanese Traditional Anti-
hemorrhoid Herb

Dear Professor Matsunami,

Thank you for submitting your manuscript to Journal of Ethnopharmacology.

I am pleased to inform you that your manuscript has been accepted for publication.

My comments, and any reviewer comments, are below.
Your accepted manuscript will now be transferred to our production department. We
will create a proof which you will be asked to check, and you will also be asked to
complete a number of online forms required for publication. If we need additional
information from you during the production process, we will contact you directly.

We appreciate you submitting your manuscript to Journal of Ethnopharmacology and
hope you will consider us again for future submissions.

Kind regards,
Prof.Dr. Erdem Yesilada
Associate Editor

Journal of Ethnopharmacology