Nama Jurnal **: Journal of Tropical Pharmacy and Chemistry (JTPC)**

Indeks **: Sinta 3**

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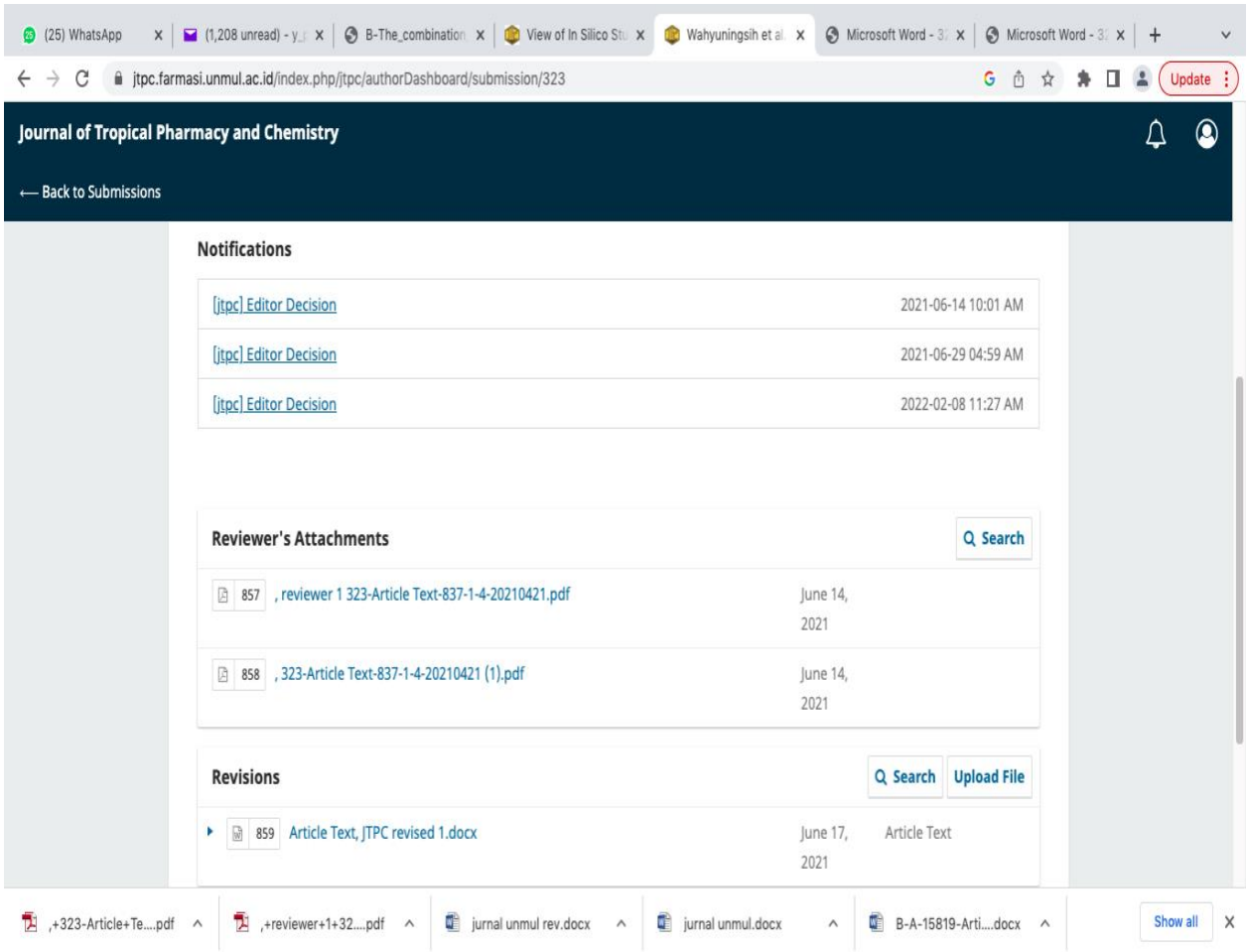
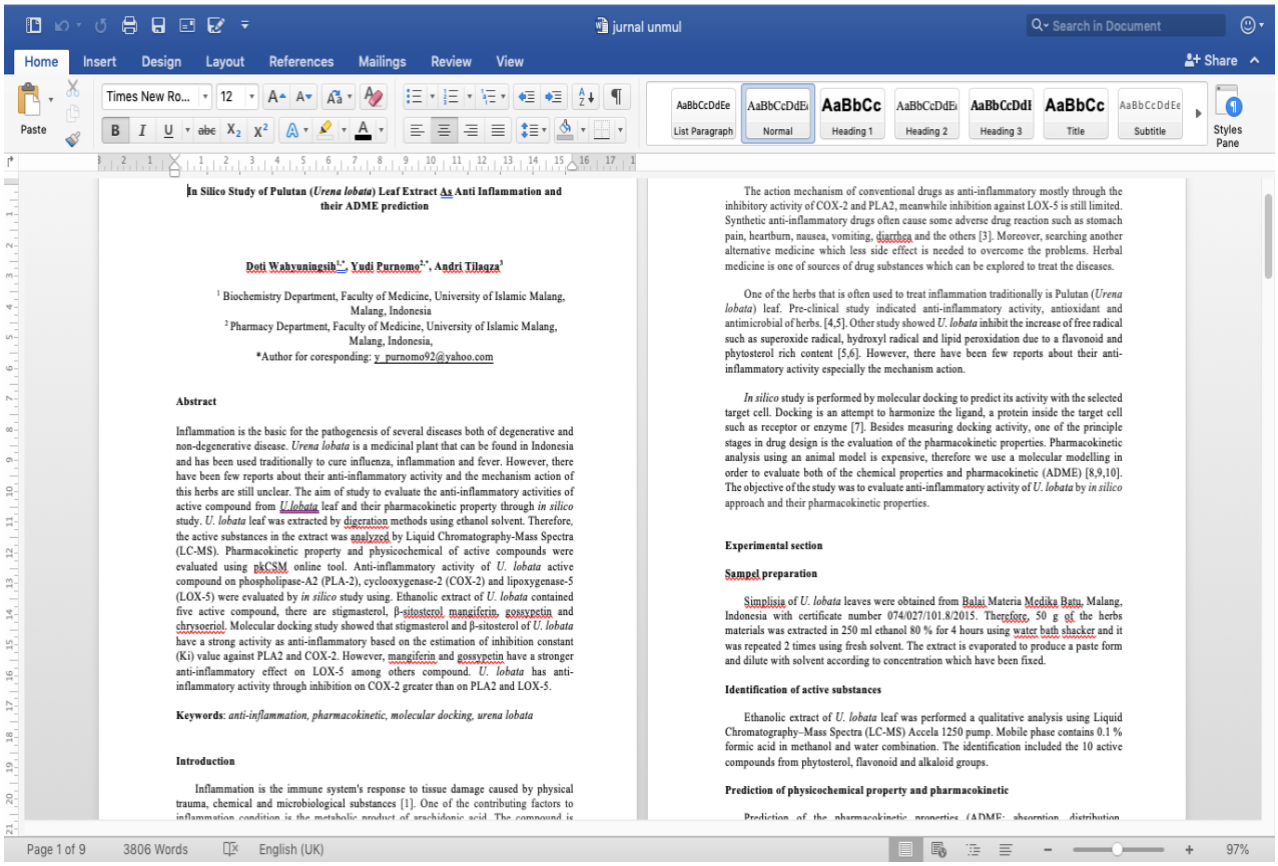
Judul Artikel : **In Silico Study of Pulutan (Urena lobata) Leaf Extract as Anti Inflammation and their ADME Prediction**

Tanggal	Activity	Reviewer Comments
31-03-2021	Submision of article	
03-02-2021	Editor responses	Article has been received by editor
14-06-2021	Editor responses	Revision of article is required
17-06-2021	Resubmit the revised article	
29-06-2021	Editor responses	Article is accepted
08-02-2021	Editor responses	Production step
29-06-2022	Editor responses	On line published



Manuscript submission



In Silico Study of Pulutan (*Urena lobata*) Leaf Extract As Anti Inflammation and their ADME prediction

Doti Wahyuningsih[1,*], Yudi Purnomo[2,*], Andri Tilaqza[3]

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[2] Pharmacy Department, Faculty of Medicine, University of Islamic Malang, Malang, Indonesia,
*Author for coresponding: y_purnomo92@yahoo.com

Abstract

Inflammation is the basic for the pathogenesis of several diseases both of degenerative and non-degenerative disease. *Urena lobata* is a medicinal plant that can be found in Indonesia and has been used traditionally to cure influenza, inflammation and fever. However, there have been few reports about their anti-inflammatory activity and the mechanism action of this herbs are still unclear. The aim of study to evaluate the anti-inflammatory activities of active compound from *U.lobata* leaf and their pharmacokinetic property through *in silico* study. *U. lobata* leaf was extracted by digeration methods using ethanol solvent. Therefore, the active substances in the extract was analyzed by Liquid Chromatography-Mass Spectra (LC-MS). Pharmacokinetic property and physicochemical of active compounds were evaluated using pkCSM online tool. Anti-inflammatory activity of *U. lobata* active compound on phospholipase-A2 (PLA-2), cyclooxygenase-2 (COX-2) and lipoxygenase-5 (LOX-5) were evaluated by *in silico* study using. Ethanolic extract of *U. lobata* contained five active compound, there are stigmasterol, β-sitosterol mangiferin, gossypetin and chrysoeriol. Molecular docking study showed that stigmasterol and β-sitosterol of *U. lobata* have a strong activity as anti-inflammatory based on the estimation of inhibition constant (Ki) value against PLA2 and COX-2. However, mangiferin and gossypetin have a stronger anti-inflammatory effect on LOX-5 among others compound. *U. lobata* has anti-inflammatory activity through inhibition on COX-2 greater than on PLA2 and LOX-5.

Keywords: *anti-inflammation, pharmacokinetic, molecular docking, urena lobata*

Introduction

Inflammation is the immune system's response to tissue damage caused by physical trauma, chemical and microbiological substances [1]. One of the contributing factors to

The action mechanism of conventional drugs as anti-inflammatory mostly through the inhibitory activity of COX-2 and PLA2, meanwhile inhibition against LOX-5 is still limited. Synthetic anti-inflammatory drugs often cause some adverse drug reaction such as stomach pain, heartburn, nausea, vomiting, diarrhea and the others [3]. Moreover, searching another alternative medicine which less side effect is needed to overcome the problems. Herbal medicine is one of sources of drug substances which can be explored to treat the diseases.

One of the herbs that is often used to treat inflammation traditionally is Pulutan (*Urena lobata*) leaf. Pre-clinical study indicated anti-inflammatory activity, antioxidant and antimicrobial of herbs. [4,5]. Other study showed *U. lobata* inhibit the increase of free radical such as superoxide radical, hydroxyl radical and lipid peroxidation due to a flavonoid and phytosterol rich content [5,6]. However, there have been few reports about their anti-inflammatory activity especially the mechanism action.

In silico study is performed by molecular docking to predict its activity with the selected target cell. Docking is an attempt to harmonize the ligand, a protein inside the target cell such as receptor or enzyme [7]. Besides measuring docking activity, one of the principle stages in drug design is the evaluation of the pharmacokinetic properties. Pharmacokinetic analysis using an animal model is expensive, therefore we use a molecular modelling in order to evaluate both of the chemical properties and pharmacokinetic (ADME) [8,9,10]. The objective of the study was to evaluate anti-inflammatory activity of *U. lobata* by *in silico* approach and their pharmacokinetic properties.

Experimental section

Sampel preparation

Simplisia of *U. lobata* leaves were obtained from Balai Materia Medika Batu, Malang, Indonesia with certificate number 074/027/101.8/2015. Therefore, 50 g of the herbs materials was extracted in 250 ml ethanol 80 % for 4 hours using water bath shacker and it was repeated 2 times using fresh solvent. The extract is evaporated to produce a paste form and dilute with solvent according to concentration which have been fixed.

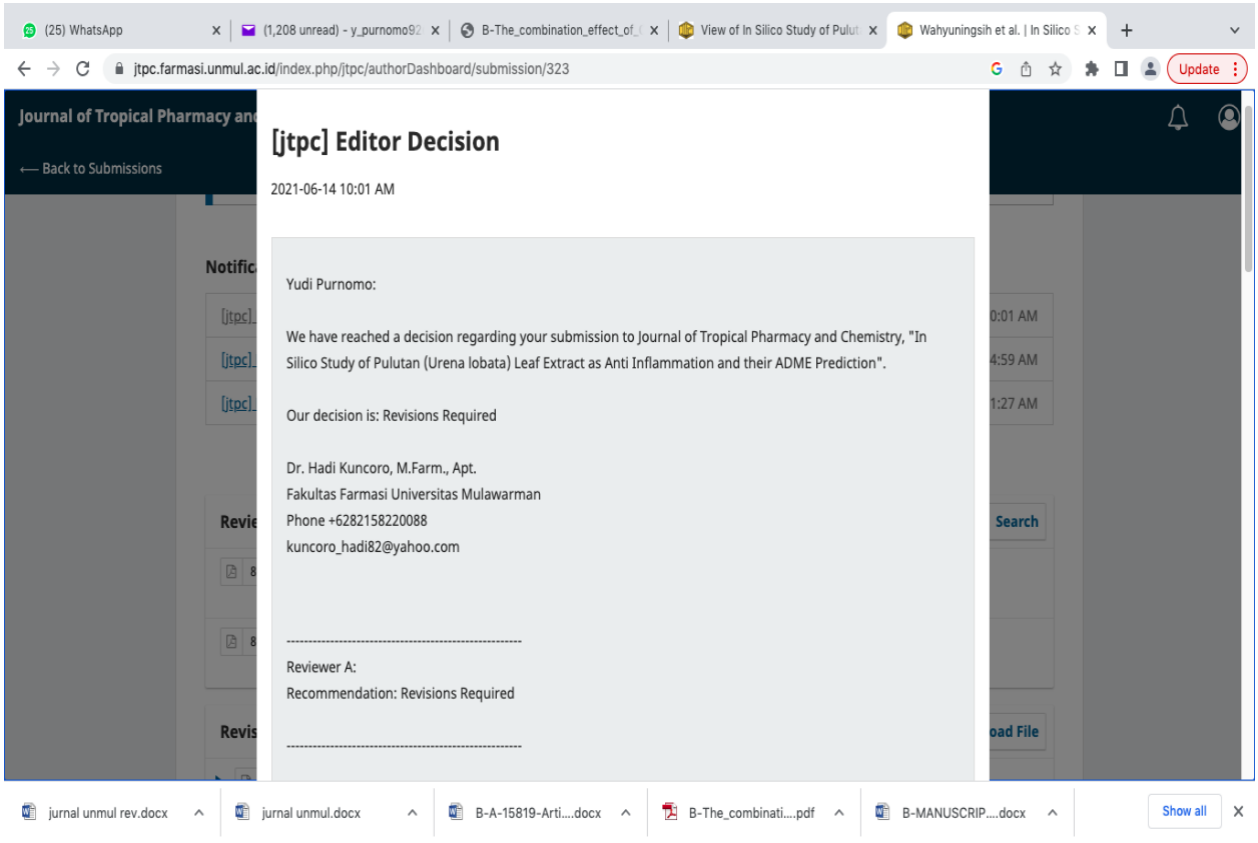
Identification of active substances

Ethanolic extract of *U. lobata* leaf was performed a qualitative analysis using Liquid Chromatography–Mass Spectra (LC-MS) Accela 1250 pump. Mobile phase contains 0.1 % formic acid in methanol and water combination. The identification included the 10 active compounds from phytosterol, flavonoid and alkaloid groups.

Prediction of physicochemical property and pharmacokinetic

Prediction of the pharmacokinetic properties (ADME: absorption, distribution

Editor Responses



[jtpc] Editor Decision

2021-06-14 10:01 AM

Yudi Purnomo:

We have reached a decision regarding your submission to Journal of Tropical Pharmacy and Chemistry, "In Silico Study of Pulutan (Urena lobata) Leaf Extract as Anti Inflammation and their ADME Prediction".

Our decision is: Revisions Required

Dr. Hadi Kuncoro, M.Farm., Apt.
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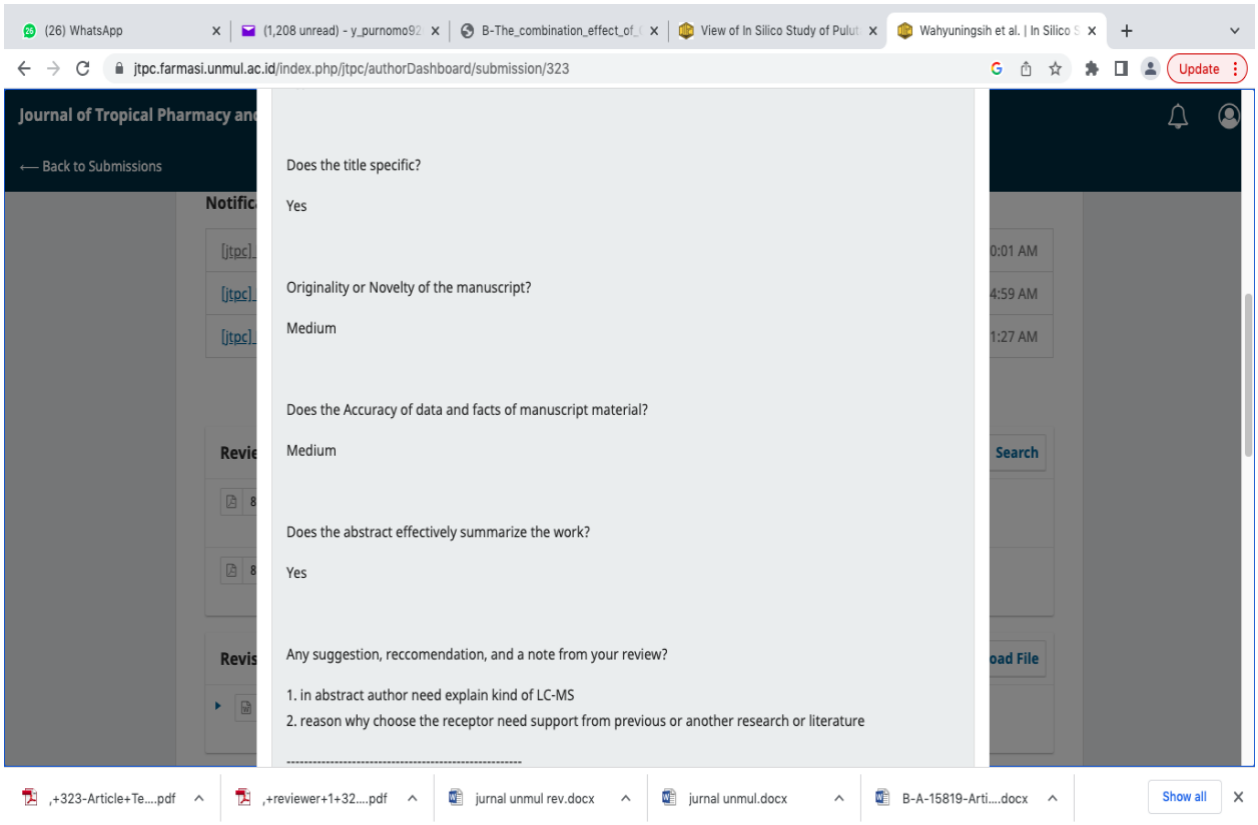
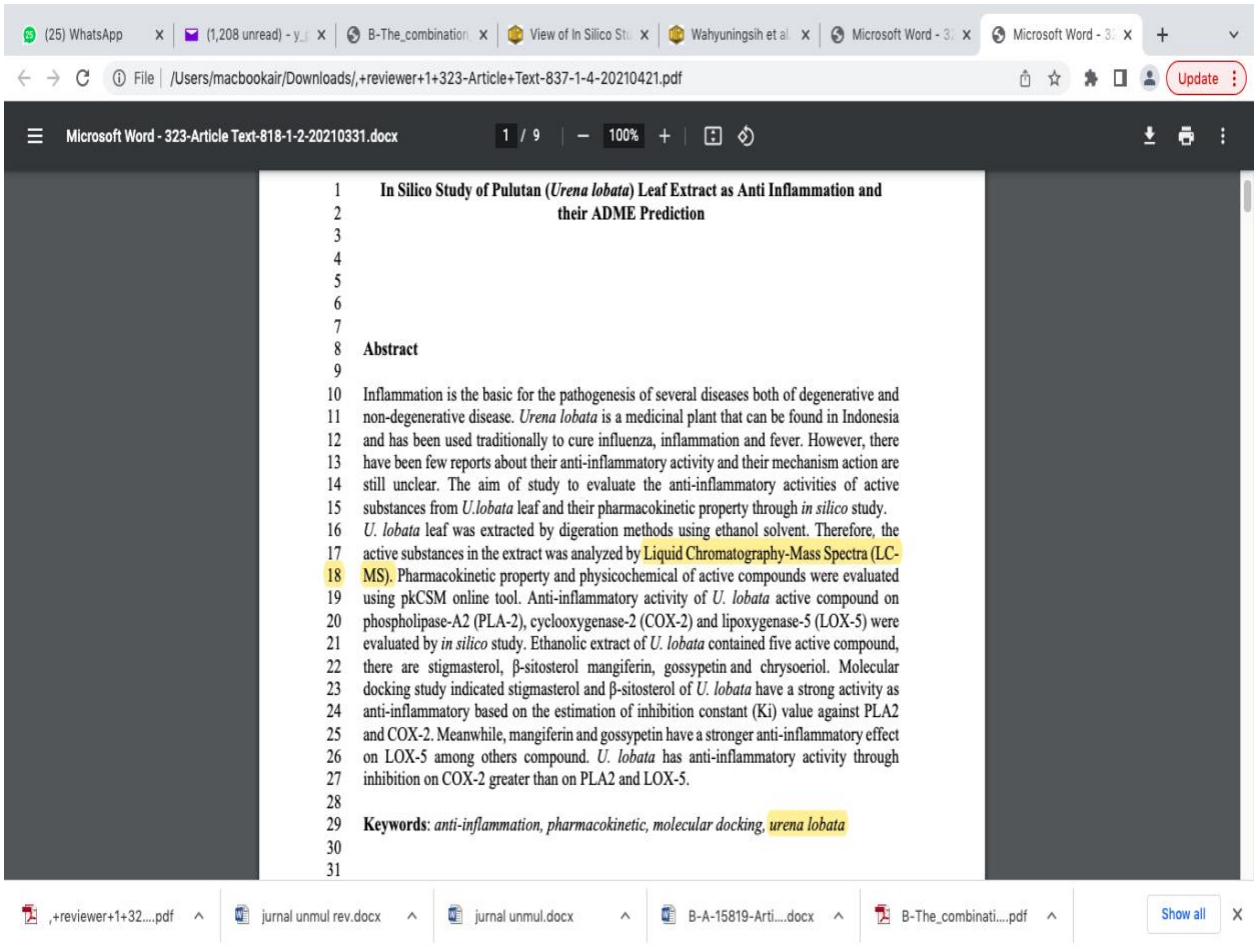
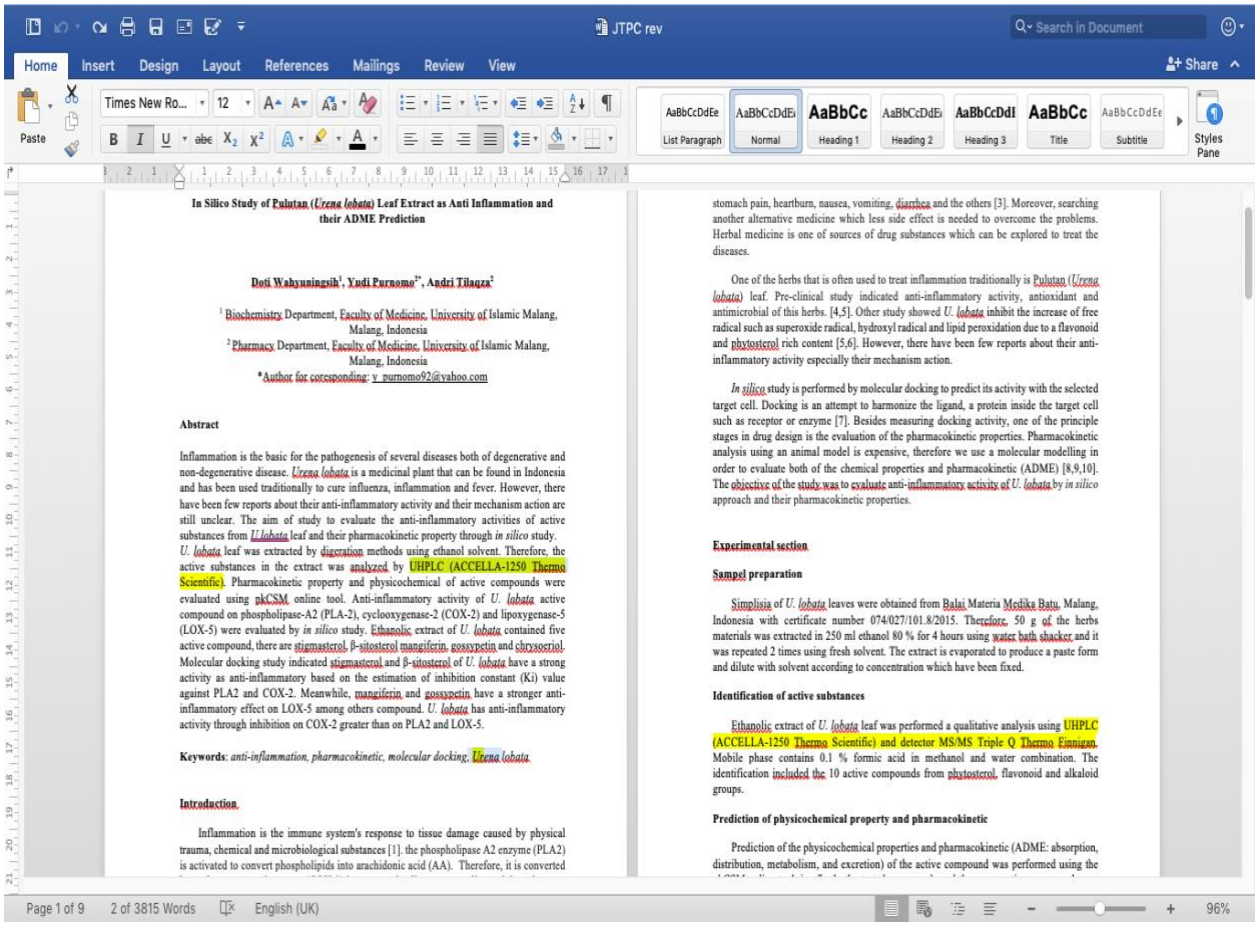
Reviewer A:
Recommendation: Revisions Required



Editor Responses



Resubmit revised manuscript



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Inflammation is the basic for the pathogenesis of several diseases both of degenerative and non-degenerative disease. *Urena lobata* is a medicinal plant that can be found in Indonesia and has been used traditionally to cure influenza, inflammation and fever. However, there have been few reports about their anti-inflammatory activity and their mechanism action are still unclear. The aim of study to evaluate the anti-inflammatory activities of active substances from *U lobata* leaf and their pharmacokinetic property through *in silico* study. *U. lobata* leaf was extracted by digeration methods using ethanol solvent. Therefore, the active substances in the extract was analyzed by UHPLC (ACCELLA-1250 Thermo Scientific). Pharmacokinetic property and physicochemical of active compounds were evaluated using pkCSM online tool. Anti-inflammatory activity of *U. lobata* active compound on phospholipase-A2 (PLA-2), cyclooxygenase-2 (COX-2) and lipoxygenase-5 (LOX-5) were evaluated by *in silico* study. Ethanolic extract of *U. lobata* contained five active compound, there are stigmasterol, β-sitosterol mangiferin, gossypetin and chrysoeriol. Molecular docking study indicated stigmasterol and β-sitosterol of *U. lobata* have a strong activity as anti-inflammatory based on the estimation of inhibition constant (Ki) value against PLA2 and COX-2. Meanwhile, mangiferin and gossypetin have a stronger anti-inflammatory effect on LOX-5 among others compound. *U. lobata* has anti-inflammatory activity through inhibition on COX-2 greater than on PLA2 and LOX-5.

Keywords: *anti-inflammation, pharmacokinetic, molecular docking, Urena lobata*

Introduction

Inflammation is the immune system's response to tissue damage caused by physical trauma, chemical and microbiological substances [1]. the phospholipase A2 enzyme (PLA2) is activated to convert phospholipids into arachidonic acid (AA). Therefore, it is converted

stomach pain, heartburn, nausea, vomiting, diarrhea and the others [3]. Moreover, searching another alternative medicine which less side effect is needed to overcome the problems. Herbal medicine is one of sources of drug substances which can be explored to treat the diseases.

One of the herbs that is often used to treat inflammation traditionally is Pulutan (*Urena lobata*) leaf. Pre-clinical study indicated anti-inflammatory activity, antioxidant and antimicrobial of this herbs. [4,5]. Other study showed *U. lobata* inhibit the increase of free radical such as superoxide radical, hydroxyl radical and lipid peroxidation due to a flavonoid and phytosterol rich content [5,6]. However, there have been few reports about their anti-inflammatory activity especially their mechanism action.

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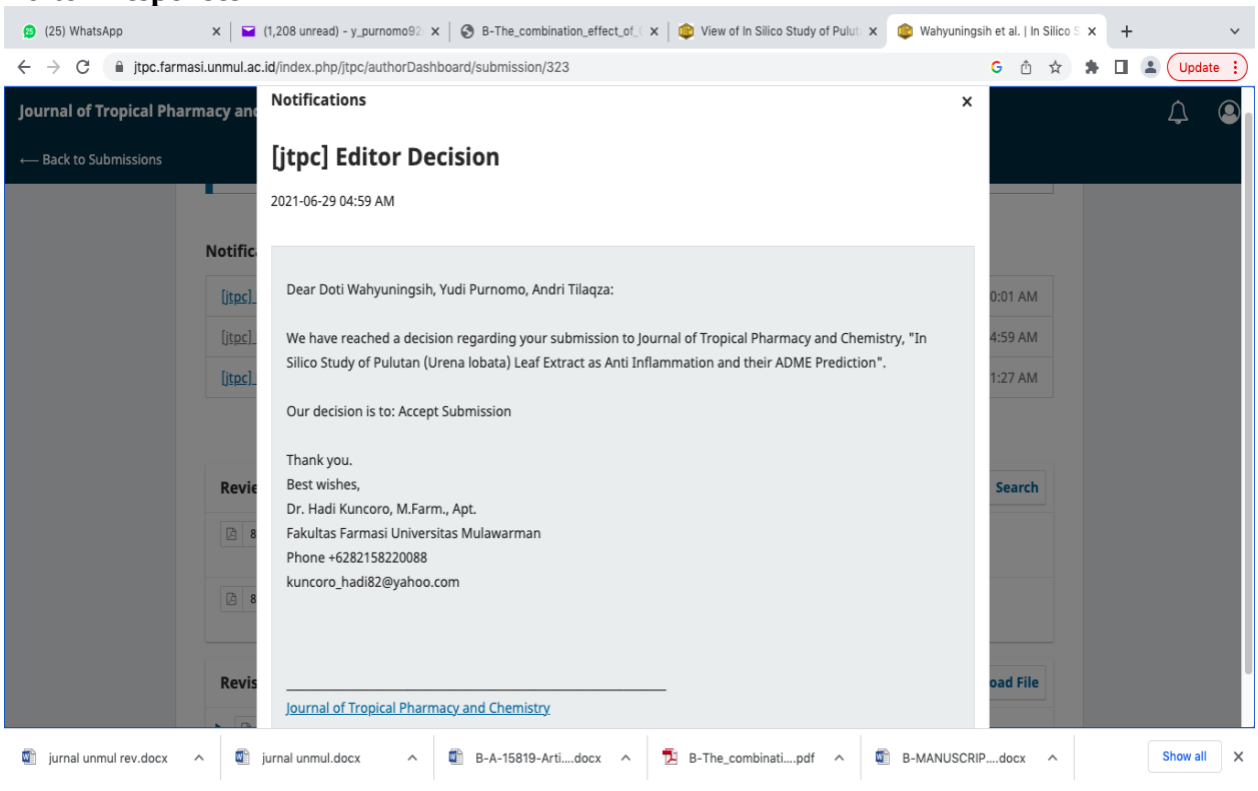
Identification of active substances

Ethanolic extract of *U. lobata* leaf was performed a qualitative analysis using UHPLC (ACCELLA-1250 Thermo Scientific) and detector MS/MS Triple Q Thermo Finnigan. Mobile phase contains 0.1 % formic acid in methanol and water combination. The identification included the 10 active compounds from phytosterol, flavonoid and alkaloid groups.

Prediction of physicochemical property and pharmacokinetic

Prediction of the physicochemical properties and pharmacokinetic (ADME: absorption, distribution, metabolism, and excretion) of the active compound was performed using the

Editor Responses



Notifications

[jtpc] Editor Decision

2021-06-29 04:59 AM

Dear Doti Wahyuningsih, Yudi Purnomo, Andri Tilaqza:

We have reached a decision regarding your submission to Journal of Tropical Pharmacy and Chemistry, "In Silico Study of Pulutan (Urena lobata) Leaf Extract as Anti Inflammation and their ADME Prediction".

Our decision is to: Accept Submission

Thank you.
Best wishes,
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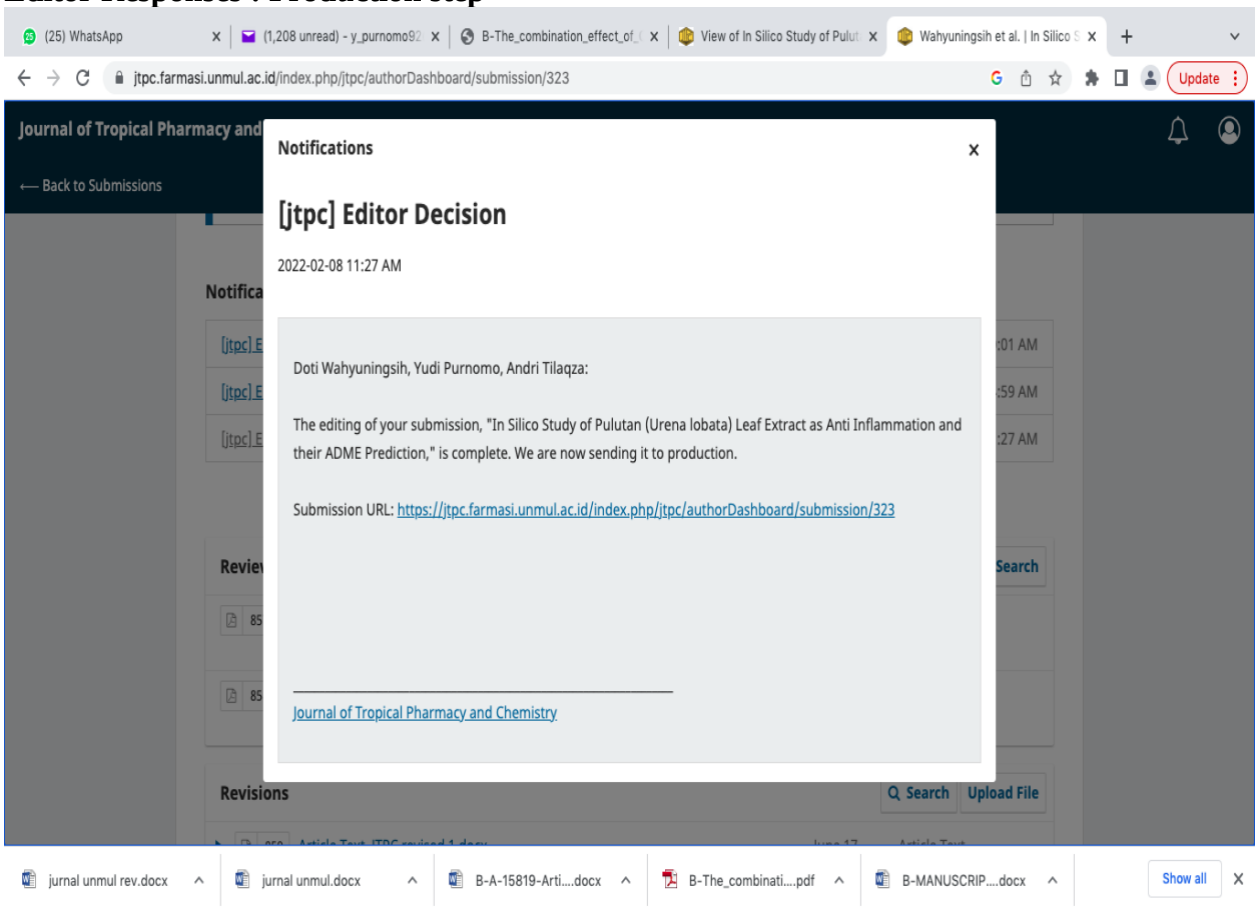
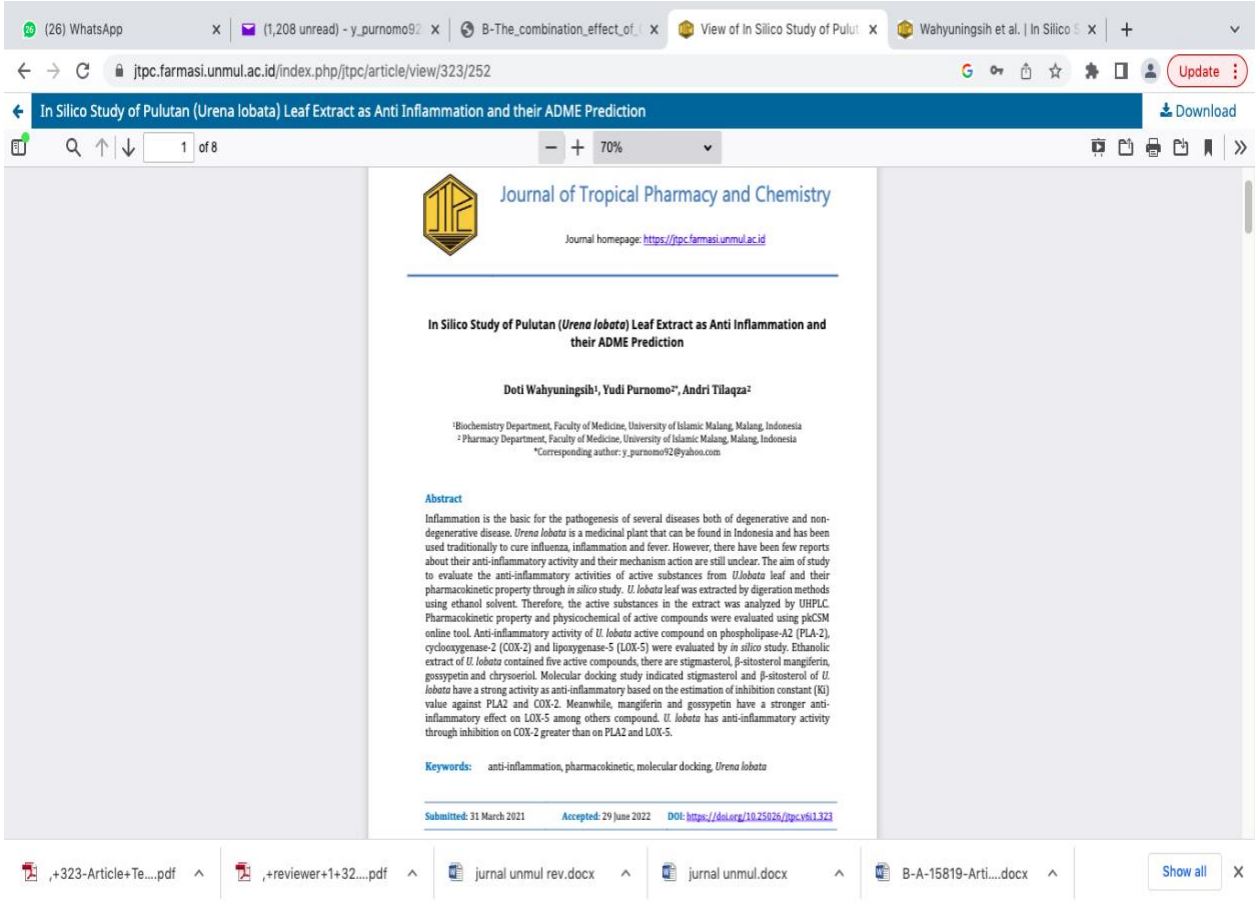
Journal of Tropical Pharmacy and Chemistry

Editor Responses : Production step



Editor Responses : On line published