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Judul Artikel **: Inhibitory activity of *Urena lobata* leaf extract on dipeptidyl peptidase-4 (DPP-4): is it different *in vitro* and *in vivo* ?**

Tanggal	Activity	Reviewer Comments
11-07-2017	Submision of article	
11-07-2017	Article received	Article has been received
22-07-2017	Editor responses	Request about four referee`s name
03-08-2017	Resubmit the revised article	
17-01-2018	Editor responses	Comments from reviewer and editor were attached
03-02-2018	Resubmit the article file	
30-01-2018	Editor responses	English editing
22-02-2018	Resubmit the revised article	
03-03-2019	Editor responses	Abstract revision
18-03-2019	Resubmit the revised article	-
17-05-2019	Galley proof sending	Galley proof correction
18-05-2019	Resubmit the revised article	-
25-05-2019	Published	On line published

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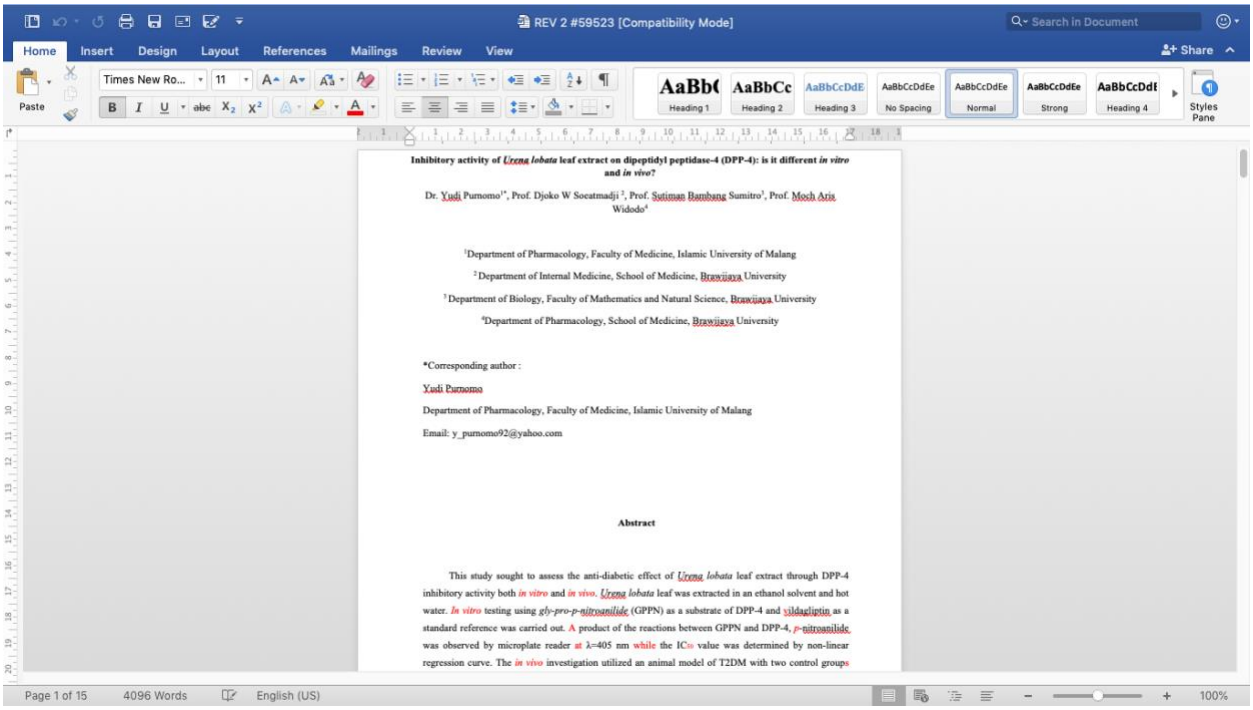

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Inhibitory activity of *Urena lobata* leaf extract on dipeptidyl peptidase-4 (DPP-4): is it different *in vitro* and *in vivo*?

Dr. Yudi Purnomo[1*], Prof. Djoko W Soeatmadji [2], Prof. Sutiman Bambang Sumitro[3], Prof. Mosh Aris Widodo[4]

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Abstract

This study sought to assess the anti-diabetic effect of *Urena lobata* leaf extract through DPP-4 inhibitory activity both *in vitro* and *in vivo*. *Urena lobata* leaf was extracted in an ethanol solvent and hot water. *In vitro* testing using *gly-pro-p-nitroanilide* (GPPN) as a substrate of DPP-4 and vildagliptin as a standard reference was carried out. A product of the reactions between GPPN and DPP-4, *p*-nitroanilide, was observed by microplate reader at λ=405 nm while the IC_{50} value was determined by non-linear regression curve. The *in vivo* investigation utilized an animal model of T2DM with two control groups

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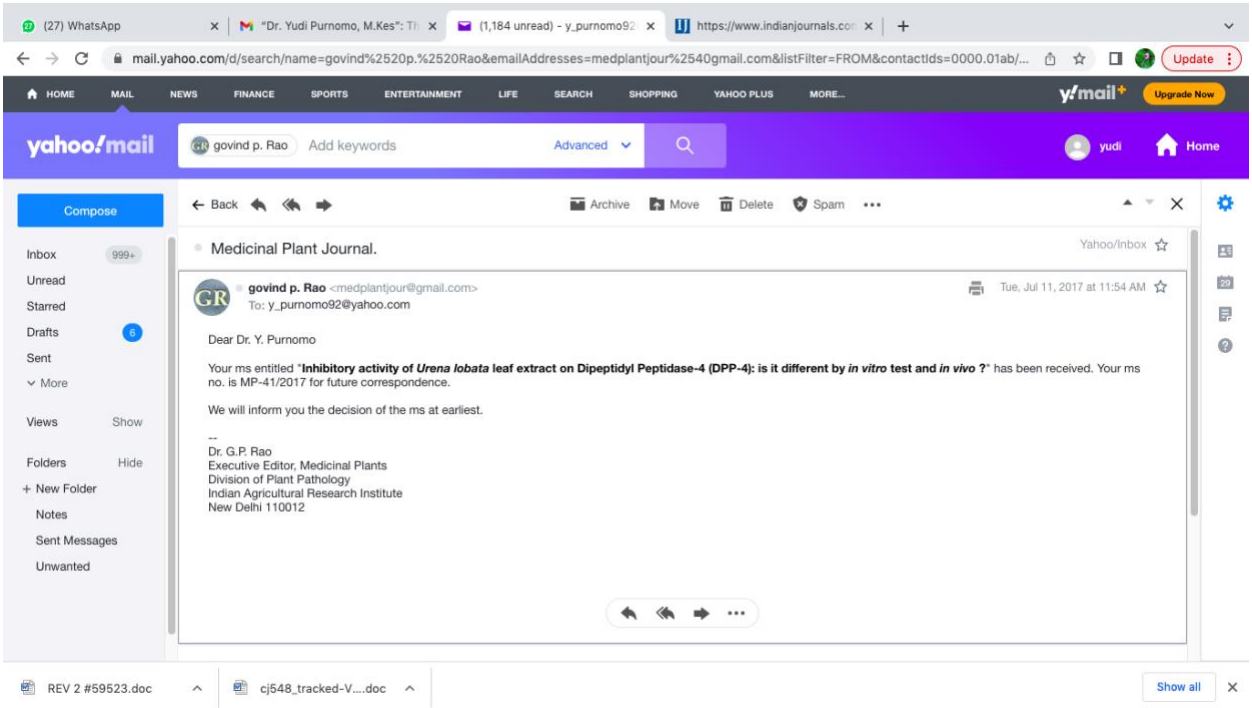

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To: y_purnomo92@yahoo.com
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Your ms entitled "**Inhibitory activity of *Urena lobata* leaf extract on Dipeptidyl Peptidase-4 (DPP-4): is it different by *in vitro* test and *in vivo* ?**" has been received. Your ms no. is MP-41/2017 for future correspondence.

We will inform you the decision of the ms at earliest.

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Dr. G.P. Rao
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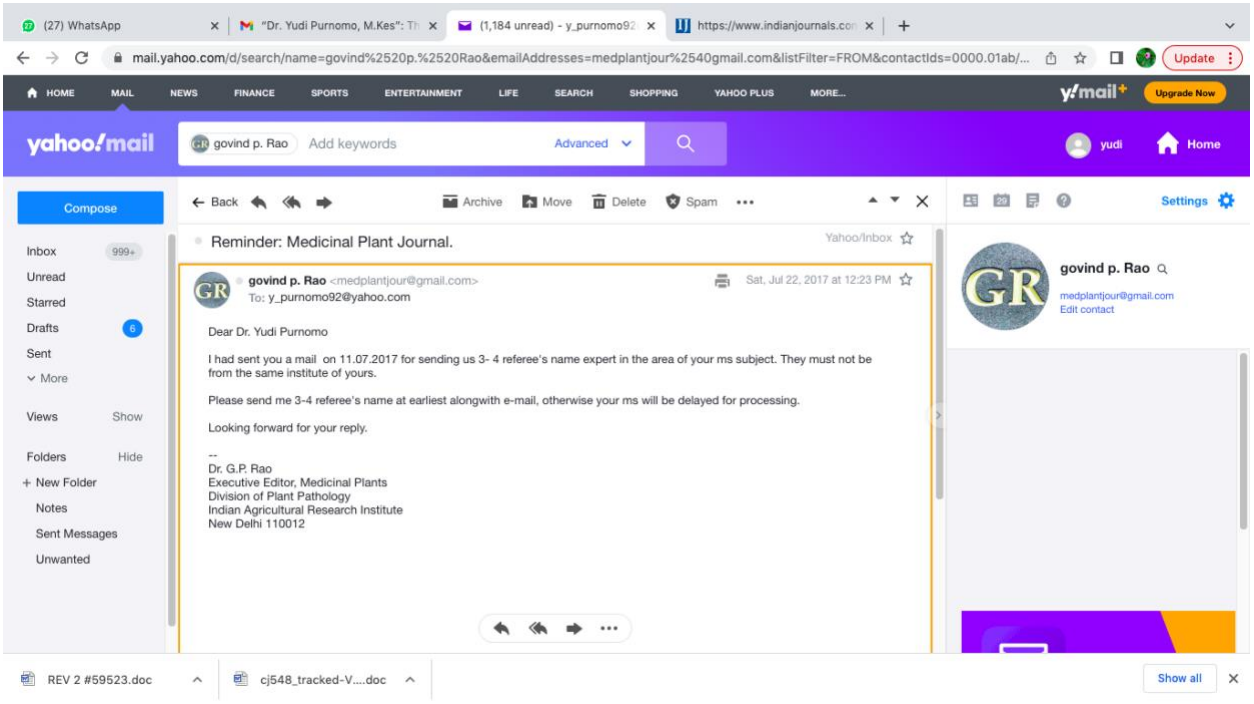

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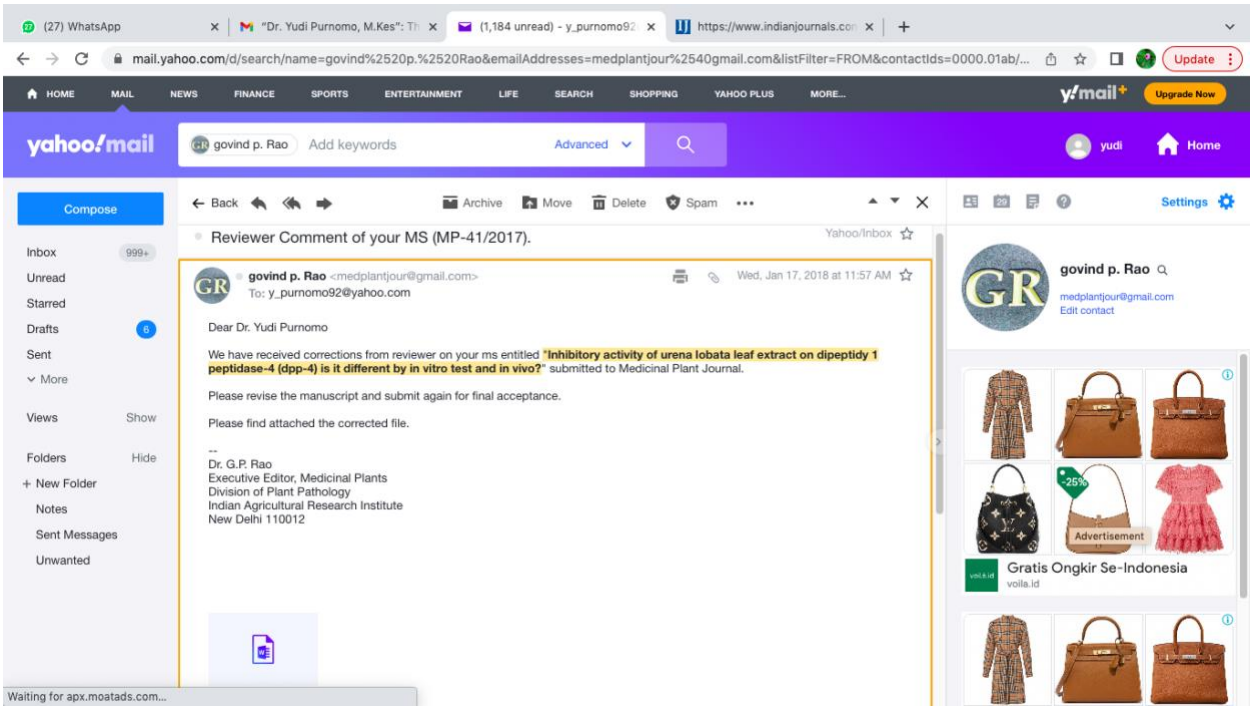

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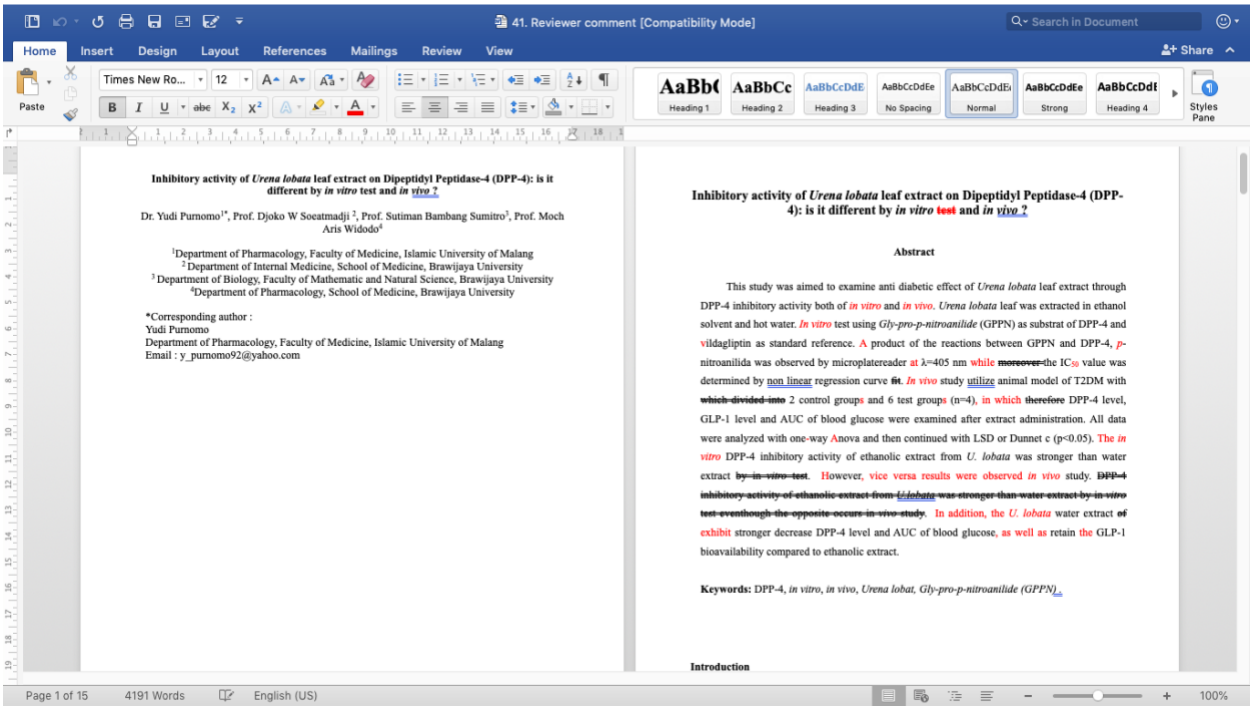

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[4]Department of Pharmacology, School of Medicine, Brawijaya University

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Keywords: DPP-4, *in vitro*, *in vivo*, *Urena lobat*, *Gly-pro-p-nitroanilide (GPPN)*,

Introduction

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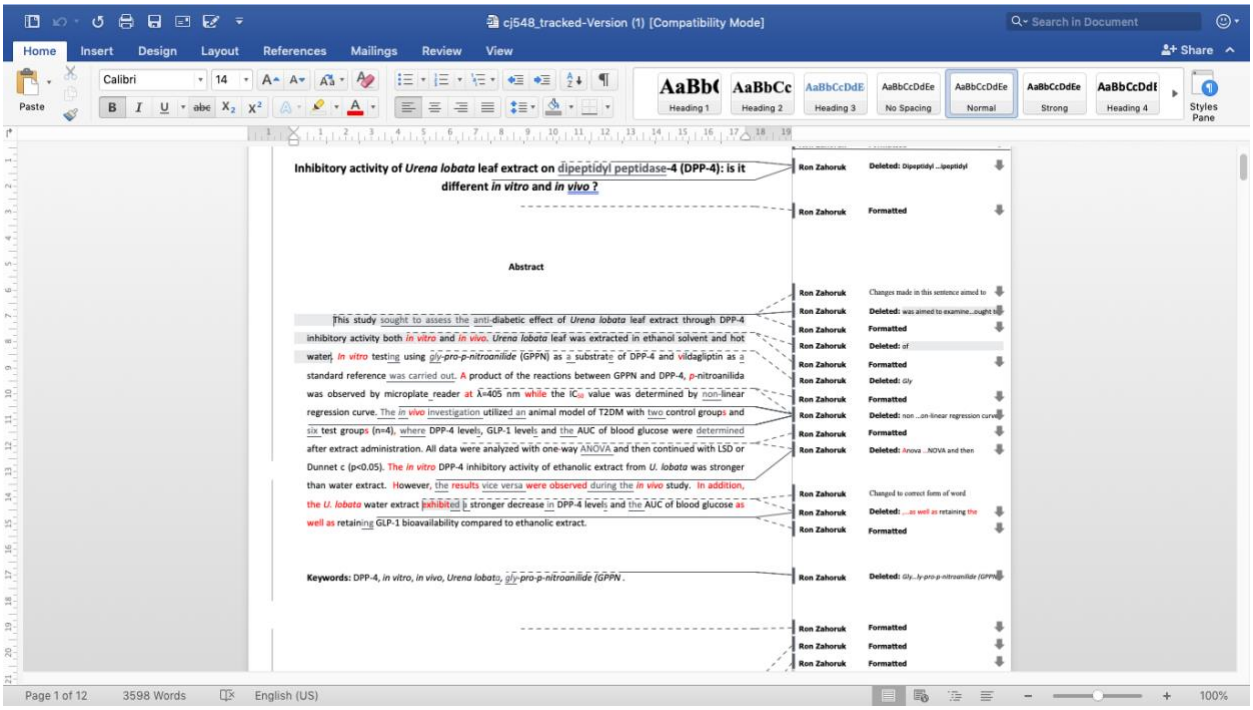

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Keywords: DPP-4, *in vitro*, *in vivo*, *Urena lobata*, *gly-pro-p-nitroanilide (GPPN)*.

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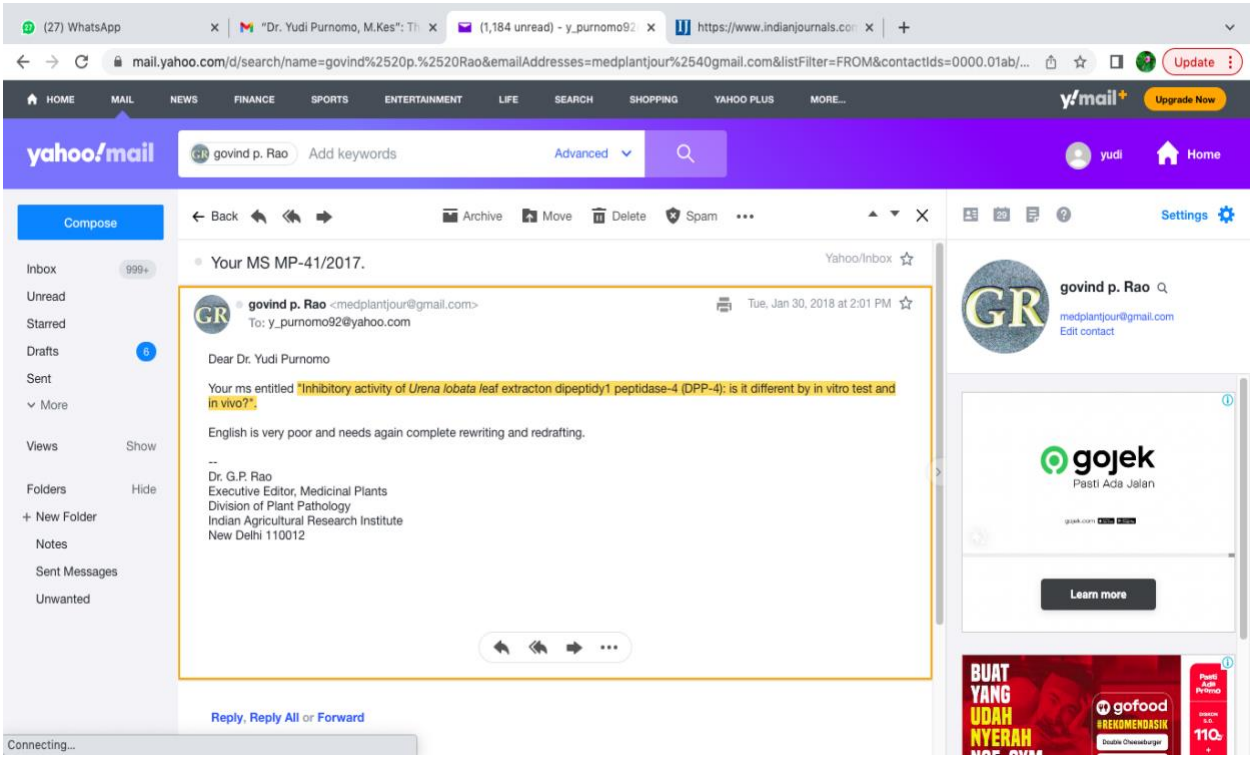

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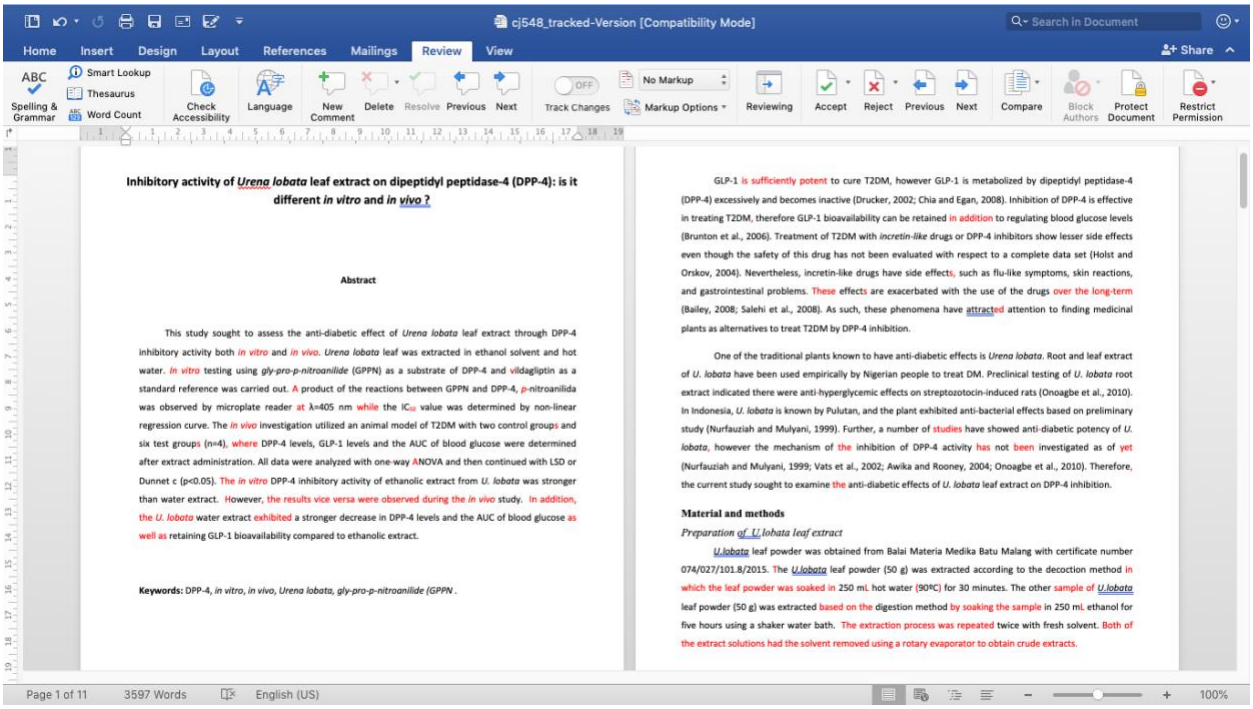

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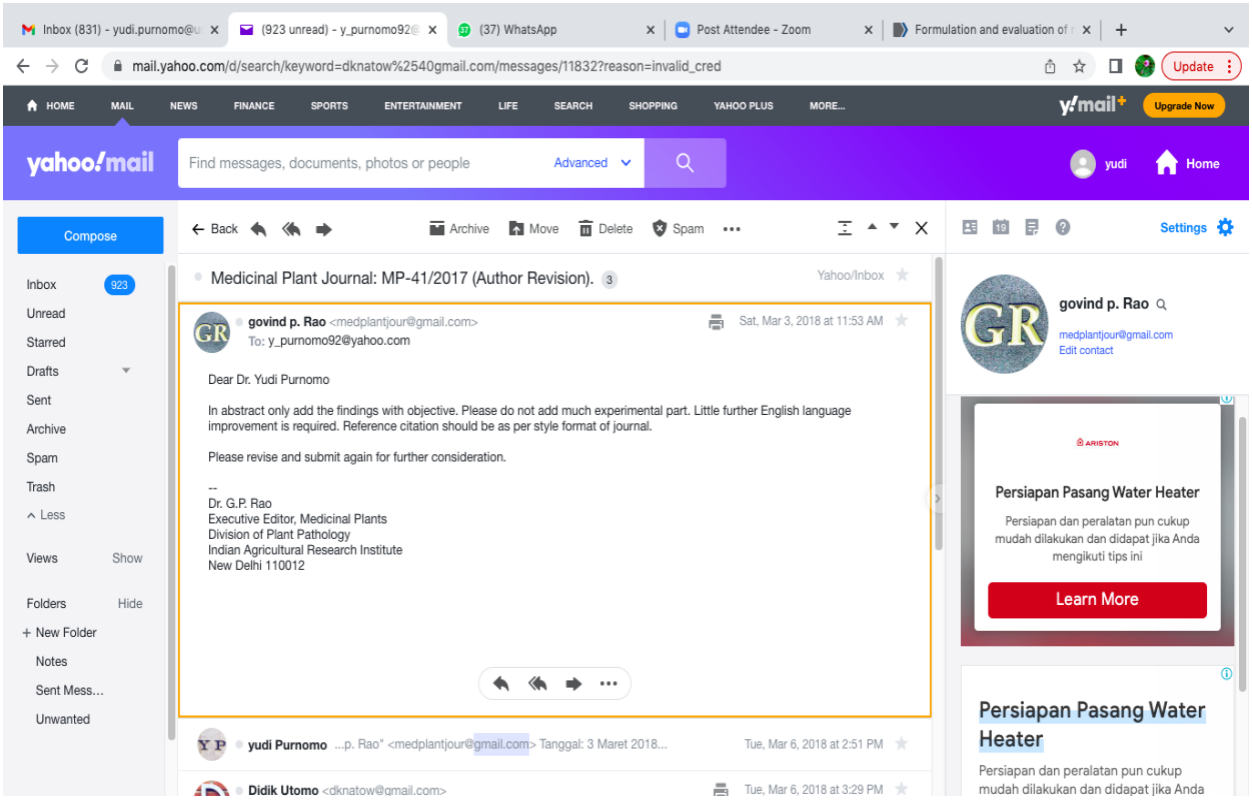

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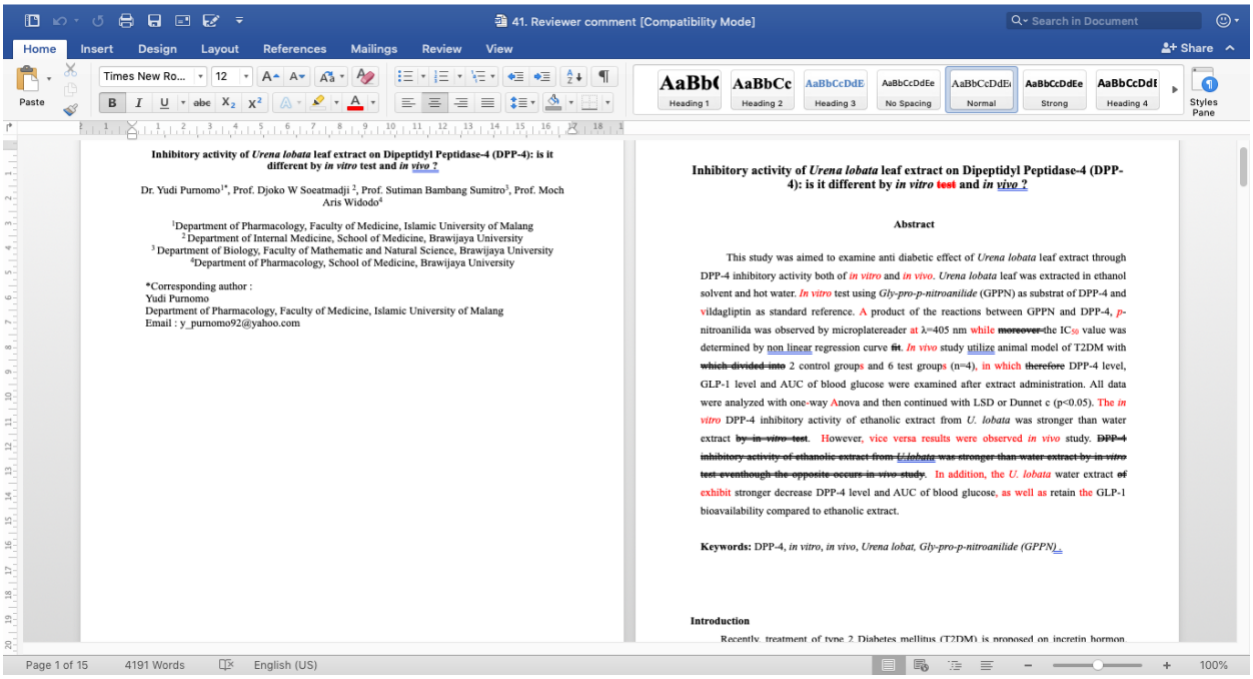

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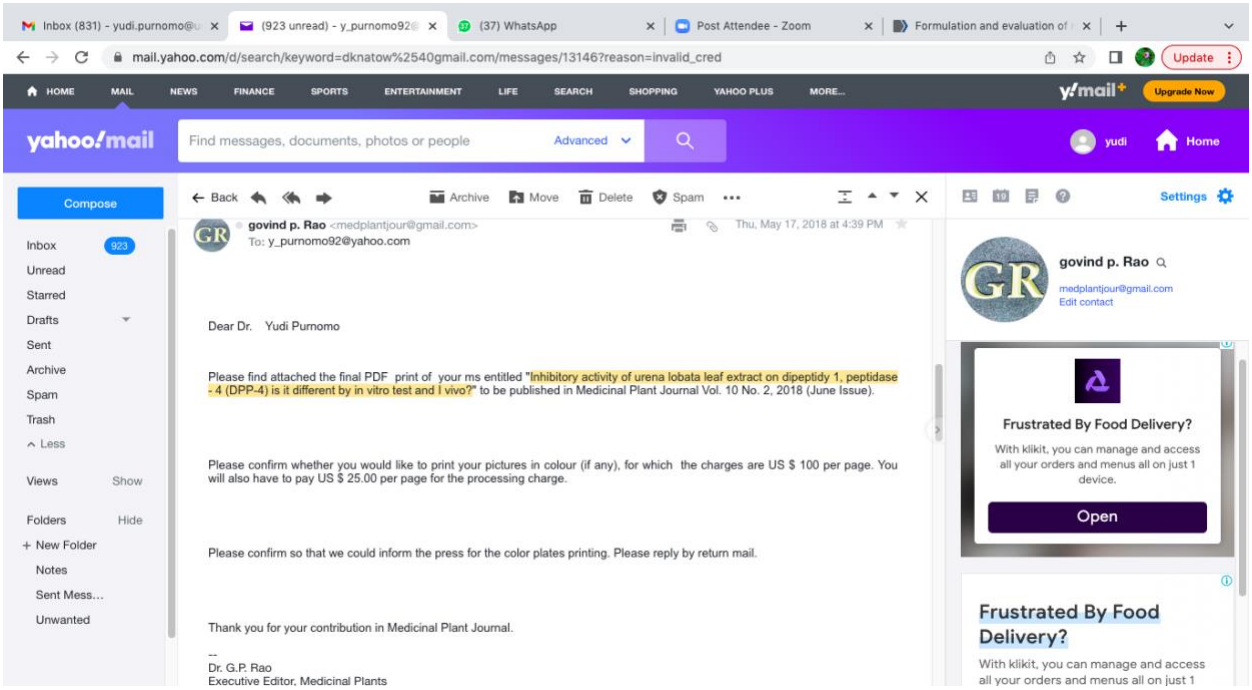

govind p. Rao <medplantjour@gmail.com>
To: y_purnomo92@yahoo.com
Thu, May 17, 2018 at 4:39 PM

Dear Dr. Yudi Purnomo

Please find attached the final PDF print of your ms entitled "Inhibitory activity of urena lobata leaf extract on dipeptidy 1, peptidase - 4 (DPP-4) is it different by in vitro test and I vivo?" to be published in Medicinal Plant Journal Vol. 10 No. 2, 2018 (June Issue).

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Research Article

Inhibitory activity of *Urena lobata* leaf extract on dipeptidyl peptidase-4 (DPP-4): is it different *in vitro* and *in vivo*?

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ABSTRACT

This study was aimed to compare the anti diabetic effect of *Urena lobata* leaf extract through DPP-4 inhibitory activity by *in vitro* and *in vivo*. *Urena lobata* leaf was extracted in ethanol and hot water to evaluate its activity on DPP-4 both of *in vitro* and *in vivo*. *In vitro* test using *Gly-pro-p-nitroanilide* (GPPN) as substrate of DPP-4 and the reactions product of them was observed by microplate reader at γ=405 nm furthermore the IC_{50} value was determined. *In vivo* study utilize an animal model of diabetes with 2 control groups and 6 test groups (n=4), in which DPP-4 level, GLP-1 level and AUC of blood glucose were examined after extract administration. The *in vitro* DPP-4 inhibitory activity of ethanolic extract of *U. lobata* is higher than water extract with the IC_{50} value of 1654,64 and 6489,88 µg/ml respectively. However, the water extract of *U. lobata* exhibits stronger decrease DPP-4 level (60-70%) compared to ethanolic extract (40-60%) *in vivo* study as well as the AUC of blood glucose were reduced by 50-60% and 20-50% respectively. Meanwhile, GLP-1 level could be retained more by the water extract of *U. lobata* administration (3-7 fold) compared to ethanolic extract (2-5 fold) due to the reducing of DPP-4 activity

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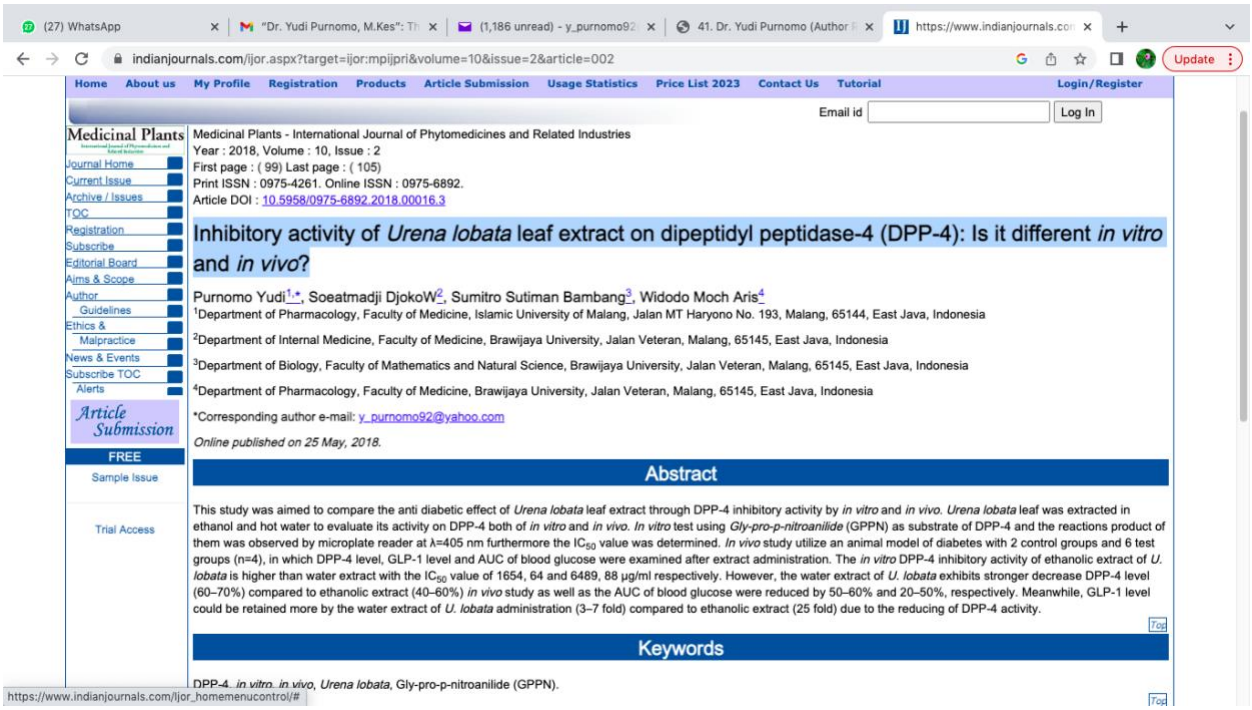

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Online published on 25 May, 2018.

Abstract

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Keywords

DPP-4, *in vitro*, *in vivo*, *Urena lobata*, Gly-pro-p-nitroanilide (GPPN).

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