

Nama Jurnal : **Medicinal Plants-International Journal of Phytomedicines and Related Industries (IJPRI)**

Indeks : **Scopus (Q4), SJR (0.14)**

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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	Submission 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

Article submission :

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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^{*}, Prof. Djoko W Soetmadji¹, Prof. Satono Bambang Sumitro¹, Prof. Moch. Aidi Widodo⁴

¹Department of Pharmacology, Faculty of Medicine, Islamic University of Malang
²Department of Internal Medicine, School of Medicine, Braujaya University
³Department of Biology, Faculty of Mathematics and Natural Science, Braujaya University
⁴Department of Pharmacology, School of Medicine, Braujaya University

*Corresponding author:
Yudi Purnomo
Department of Pharmacology, Faculty of Medicine, Islamic University of Malang
Email: y_purnomo92@yahoo.com

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-nitroamides* (GPPN) as a substrate of DPP-4 and sildaglifin as a standard reference was carried out. A product of the reactions between GPPN and DPP-4, *p-nitroamides*, was observed by microplate reader at $\lambda=405$ 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.

Page 1 of 15 4096 Words English (US) 100%

Article received by editor :

(27) WhatsApp x "Dr. Yudi Purnomo, M.Kes": T... x (1,184 unread) - y_purnomo92 x https://www.indianjournals.com x +

mail.yahoo.com/d/search/name=govind%2520p.%2520Rao&emailAddresses=medplantjour%2540gmail.com&listFilter=FROM&contactIds=0000.01ab/... Update

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Medicinal Plant Journal. Yahoo/Inbox

govind p. Rao <medplantjour@gmail.com> Tue, Jul 11, 2017 at 11:54 AM

To: y_purnomo92@yahoo.com

Dear Dr. Y. Purnomo

Your ms entitled 'Inhibitory activity of *Urena lobata* leaf extract on Dipeptidyl Peptidase-4 (DPP-4): is it different *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.

—
Dr. G.P. Rao
Executive Editor, Medicinal Plants
Division of Plant Pathology
Indian Agricultural Research Institute
New Delhi 110012

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Editor comments :

The screenshot shows a Yahoo! Mail interface. The search bar contains "govind p. Rao". The email is titled "Reminder: Medicinal Plant Journal." and is dated "Sat, Jul 22, 2017 at 12:23 PM". The sender is "govind p. Rao" with the email address "medplantjour@gmail.com". The recipient is "y_purnomo92@yahoo.com". The body of the email reads: "Dear Dr. Yudi Purnomo I had sent you a mail on 11.07.2017 for sending us 3- 4 referee's name expert in the area of your ms subject. They must not be from the same institute of yours. Please send me 3-4 referee's name at earliest alongwith e-mail, otherwise your ms will be delayed for processing. Looking forward for your reply. -- Dr. G.P. Rao Executive Editor, Medicinal Plants Division of Plant Pathology Indian Agricultural Research Institute New Delhi 110012". The right sidebar shows the sender's profile with a "GR" logo and contact information. At the bottom, there are file attachments: "REV 2 #59523.doc" and "cj548_tracked-V....doc".

Reviewer comments :

The screenshot shows a Yahoo! Mail interface. The search bar contains "govind p. Rao". The email is titled "Reviewer Comment of your MS (MP-41/2017)." and is dated "Wed, Jan 17, 2018 at 11:57 AM". The sender is "govind p. Rao" with the email address "medplantjour@gmail.com". The recipient is "y_purnomo92@yahoo.com". The body of the email reads: "Dear Dr. Yudi Purnomo We have received corrections from reviewer on your ms entitled 'Inhibitory activity of urena lobata leaf extract on dipeptidyl 1 peptidase-4 (dpp-4) is it different by in vitro test and in vivo?' submitted to Medicinal Plant Journal. Please revise the manuscript and submit again for final acceptance. Please find attached the corrected file. -- Dr. G.P. Rao Executive Editor, Medicinal Plants Division of Plant Pathology Indian Agricultural Research Institute New Delhi 110012". The right sidebar shows the sender's profile with a "GR" logo and contact information. Below the profile, there is an advertisement for "Gratis Ongkir Se-Indonesia" from "volia.id" featuring various handbags. At the bottom left, there is a status bar that says "Waiting for apx.moads.com...".

Reviewer comments :

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Dr. Yudi Purnomo¹, Prof. Djoko W Soetmadji², Prof. Sutiman Bambang Sumitro³, Prof. Moch Aris Widodo⁴

¹Department of Pharmacology, Faculty of Medicine, Islamic University of Malang
²Department of Internal Medicine, School of Medicine, Brawijaya University
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*Corresponding author :
Yudi Purnomo
Department of Pharmacology, Faculty of Medicine, Islamic University of Malang
Email : y_purnomo92@yahoo.com

Inhibitory activity of *Urena lobata* leaf extract on Dipeptidyl Peptidase-4 (DPP-4): is it different by *in vitro* test and *in vivo* ?

Abstract

This study was aimed to examine anti diabetic effect of *Urena lobata* leaf extract through DPP-4 inhibitory activity both of *in vitro* and *in vivo*. *Urena lobata* leaf was extracted in ethanol solvent and hot water. *In vitro* test using *Gly-pro-p-nitroanilide* (GPPN) as substrat of DPP-4 and *vildagliptin* as standard reference. A product of the reactions between GPPN and DPP-4, *p-nitroanilida* was observed by microplate reader at $\lambda=405$ nm while ~~however~~ the IC_{50} value was determined by non linear regression curve fit. *In vivo* study utilize animal model of T2DM with which divided into 2 control groups and 6 test groups (n=4), in which therefore DPP-4 level, GLP-1 level and AUC of blood glucose were examined after extract administration. All data were analyzed with one-way Anova and then continued with LSD or Dunnet c (p<0.05). The *in vitro* DPP-4 inhibitory activity of ethanolic extract from *U. lobata* was stronger than water extract by *in vitro* test. However, vice versa results were observed *in vivo* study. ~~DPP-4 inhibitory activity of ethanolic extract from *U.lobata* was stronger than water extract by *in vitro* test even though the opposite occurs *in vivo* study.~~ In addition, the *U. lobata* water extract of exhibit stronger decrease DPP-4 level and AUC of blood glucose, as well as retain the GLP-1 bioavailability compared to ethanolic extract.

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

Introduction

Page 1 of 15 4191 Words English (US) 100%

Resubmit article revised :

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

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Page 1 of 12 3598 Words English (US) 100%

Reviewer comments (English Editing) :

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English edited of manuscript:

Page 1 of 11 3597 Words English (US) 100%

Editor comments :

The screenshot shows a Yahoo! Mail inbox with an email from Dr. G.P. Rao. The email content is as follows:

Dear Dr. Yudi Purnomo

In abstract only add the findings with objective. Please do not add much experimental part. Little further English language improvement is required. Reference citation should be as per style format of journal.

Please revise and submit again for further consideration.

--
Dr. G.P. Rao
Executive Editor, Medicinal Plants
Division of Plant Pathology
Indian Agricultural Research Institute
New Delhi 110012

The email is dated Sat, Mar 3, 2018 at 11:53 AM. Below the email, a reply from Yudi Purnomo is partially visible, dated Tue, Mar 6, 2018 at 2:51 PM.

Abstract revised :

The screenshot shows a Microsoft Word document with the following abstract text highlighted in yellow:

Inhibitory activity of *Urena lobata* leaf extract on Dipeptidyl Peptidase-4 (DPP-4): is it different by *in vitro* test and *in vivo* ?

Dr. Yudi Purnomo¹, Prof. Djoko W Soetmadji², Prof. Sutiman Bambang Sumitro³, Prof. Moeh Artis Widodo⁴

¹Department of Pharmacology, Faculty of Medicine, Islamic University of Malang
²Department of Internal Medicine, School of Medicine, Brawijaya University
³Department of Biology, Faculty of Mathematic and Natural Science, Brawijaya University
⁴Department of Pharmacology, School of Medicine, Brawijaya University

*Corresponding author :
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Department of Pharmacology, Faculty of Medicine, Islamic University of Malang
Email : y_purnomo92@yahoo.com

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

Introduction

Recently, treatment of type 2 Diabetes mellitus (T2DM) is nonoson on incretin hormon

Editor comments :

Inbox (831) - yudi.purnomo@... x (923 unread) - y_purnomo92@... x (37) WhatsApp x Post Attendee - Zoom x Formulation and evaluation of... x +

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GR 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 dipeptidyl 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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Thank you for your contribution in Medicinal Plant Journal.

Dr. G.P. Rao
Executive Editor, Medicinal Plants

GR govind p. Rao medplantjour@gmail.com Edit contact

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Medicinal Plants Vol. 10 (2), June 2018, 91-97 doi: IndianJournals.com

Research Article

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

Yudi Purnomo*, Djoko W Soetmadji¹, Sutiman Bambang Sumitro² and Moch Aris Widodo⁴
¹Department of Pharmacology, Faculty of Medicine, Islamic University of Malang, Jalan MT Hariyono No. 193, Malang 65144, East Java, Indonesia
²Department of Internal Medicine, Faculty of Medicine, Brawijaya University, Jalan Veteran, Malang 65145, East Java, Indonesia
³Department of Biology, Faculty of Mathematics and Natural Science, Brawijaya University, Jalan Veteran, Malang 65145, East Java, Indonesia
⁴Department of Pharmacology, Faculty of Medicine, Brawijaya University, Jalan Veteran, Malang 65145, East Java, Indonesia

Received: ; Accepted:

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-nitrosanilide* (GPPN) as substrate of DPP-4 and the reactions product of them was observed by microplate reader at $\gamma=405$ 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 μ g/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.

On line published :

The screenshot shows a web browser window with the URL <https://www.indianjournals.com/ijor.aspx?target=ijor:mpijpri&volume=10&issue=2&article=002>. The page is for the journal "Medicinal Plants - International Journal of Phytomedicines and Related Industries". The article title is "Inhibitory activity of *Urena lobata* leaf extract on dipeptidyl peptidase-4 (DPP-4): Is it different *in vitro* and *in vivo*?". The authors are Purnomo Yudi^{1,*}, Soeatmadji DjokoW², Sumitro Sutiman Bambang³, and Widodo Moch Aris⁴. The abstract states: "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 $\lambda=405$ 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 $\mu\text{g/ml}$ 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 (25 fold) due to the reducing of DPP-4 activity." The keywords are "DPP-4, *in vitro*, *in vivo*, *Urena lobata*, Gly-pro-p-nitroanilide (GPPN)".