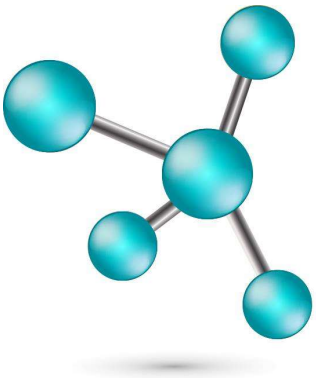


ASIA PACIFIC JOURNAL OF
MOLECULAR BIOLOGY & BIOTECHNOLOGY

Volume 28; 2020 (/index.php/archive-issues/18-apjmbb/451-archive-issue-28)

Volume 28 (1); 2020

Nuclease pre-treatment increases efficiency of whole genome sequencing of Influenza B vir

Wudtichai Manasatienkij, Piyawan Chinnawirotpisan, Weerayuth Kittichotirat, Sriluck Simasathien, Ellison, Supapon Cheevadhanarak, Wiriya Rutvisuttinunt, Stefan Fernandez, Chonticha Klungthon

APJMBB 28 (1): 1-13

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.01 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/01-Manasatienkij-et-al.pdf)]

Potential use of *Pennisetum purpureum* for phytoremediation and bioenergy production: a r

Nurul Atiqah Osman, Ahmad Muhaimin Roslan, Mohamad Faizal Ibrahim, Mohd Ali Hassan

(/)

APJMBB 28 (1): 14-26

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.02 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/02-Osman-et-al.pdf)]

Plasma miR-126 levels and its genomic polymorphism SNP rs4636297 in Type 2 diabetes

Monireh Rezai, Shirin Shahbazi, Nasrin Mansournia

APJMBB 28 (1): 27-33

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.03 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/03-Rezai-et-al.pdf)]

In-silico molecular docking study of novel derivatives of erlotinib in glioma

Deepika Tripathi, Sabiha Imran

APJMBB 28 (1): 33-38

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.04 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/04-Tripathi-et-al.pdf)]

Transcriptome analysis of *Phytophthora infestans* and *Colletotrichum coccodes* in tomato t

Abbas Saidi, Zahra Hajibarat, Zohreh Hajibarat

APJMBB 28 (1): 39-51

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.05 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/05-Saidi-et-al.pdf)]

Development of attenuated *Vibrio parahaemolyticus* mutant strains as potential live vaccine

Vu Thi Bich Huyen, Nguyen Xuan Viet, Pham Thi Tam, Man Hong Phuoc, Huynh Viet Tung, Nguye

APJMBB 28 (1): 52-67

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.06 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/06-Huyen-et-al.pdf)]

Statistical optimization of an acid protease production by a local *Aspergillus niger*MH10954 decommissioned dates

Malika Benkahoul, Amina Bramki, Aicha Belmessikh, Aicha Mechakra-Maza

APJMBB 28 (1): 68-76

(/)

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.07 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/07-Benkahoul-et-al.pdf)]

Mini review on phenol biodegradation in Antarctica using native microorganisms

Kavilasni Subramaniam, Siti Aqlima Ahmad, Noor Azmi Shaharuddin

APJMBB 28 (1): 77-89

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.08 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/08-Subramaniam-et-al.pdf)]

Trihoney ameliorates hypercholesterolemia-induced epididymal histopathological changes

Zenab B. Hamad Mohamed, Muhammad Bin Ibrahim, Hamad Abdulsalam Hamad Alfarisi, Azantee Fuaat, Che Anuar Che Mohamad

APJMBB 28 (1): 690-100

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.09 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/09-Hamad-Mohamed-et-al.p

Prediction of B-cell epitope by *in silico* analysis of *Mycobacterium tuberculosis* Ag85B antig

Nihayatul Karimah, Sabar Pambudi

APJMBB 28 (1): 101-109

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.10 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/10-Karimah-et-al.pdf)]

Stevia: limiting cholesterol synthesis in Hep-G2 cells

Amirul Nazhan Ilias, Hazilawati Hamzah, Intan Safinar Ismail, Mokrish Ajat

APJMBB 28 (1): 110-119

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.1.11 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_1/11-Ilias-et-al.pdf)] [Supplem (/images/publication/volume_28/issue_1/Supplemental_Ilias-et-al.pdf)]

Volume 28 (2); 2020

Mechanism and challenges associated with adaptation and evolution of drug-resistant bact

Shikha Kapil, Tarun Kumar, Vipasha Sharma

APJMBB 28 (2): 1-18

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.01 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/01-Kapil-et-al.pdf)]

Taxonomic note: speciation within the operational group *Bacillus amyloliquefaciens*based o housekeeping genes

Mohamad Syazwan Ngalimat, Suriana Sabri

APJMBB 28 (2): 19-26

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.02 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/02-Ngalimat-et-al.pdf)] [Supp (/images/publication/volume_28/issue_2/Supplemental_Ngalimat.pdf)]

Insertion/deletion of angiotensin-converting enzyme gene polymorphism as a marker of pol development in South Indian cohort women

Nishu Sekar, Abilash Valsala Gopalakrishnan

APJMBB 28 (2): 27-31

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.03 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/03-Sekar-et-al.pdf)]

Microencapsulation of *Bifidobacterium animalis* subsp. *lactis* BB-12 with mannitol

Agnes Kai Lin Yong, Ka Wai Lai, Hasanah Mohamad Ghazali, Lee Sin Chang, Liew Phing Pui

APJMBB 28 (2): 32-42

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.04 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/04-Yong-et-al.pdf)]

Analysis of mRNA expression and DNA methylation level of RAC1 gene encoding focal adh peritoneal endometriosis

Irwina Eka Deraya, Andon Hestiantoro, Raden Muharam, Muhammad Lucky Marwali, Agus Surur A Gita Pratama, Ocktariyana, Annisah Zahrah, Asmarinah

APJMBB 28 (2): 43-49

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.05 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/05-Deraya-et-al.pdf)]

Effect of *Acacia* purified tannins extract and polyethylene glycol treatment on *in vitro* rumina production

Khaoula Khelalfa, Rabah Arhab, Antonio Ignacio Martín-García, Nabila Zaabat, Alejandro Belanch

APJMBB 28 (2): 45-62

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.06 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/06-Khelalfa-et-al.pdf)]

Assessment of growth and phytochemical quality of *Gynura procumbens* through nitrogen, evapotranspiration replacement interaction

Mohamad Fhaizal Mohamad Bukhori, Hawa ZE Jaafar, Ali Ghasemzadeh, Uma Rani Sinniah, Gay

APJMBB 28 (2): 63-91

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.07 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/07-Mohamad-Bukhori-et-al.p

Reproductive development of the priapium fish *Neosthetus lankesteri* Regan, 1916 (Atherini Pranburi river estuary, Thailand using the histological approach

Amphornphan Palasai, Sinlapachai Senarat, Phakorn Na Lampang, Niwat Kangwanrangsan, Wan de Sequiera-Silva, Jes Kettratad

APJMBB 28 (2): 92-104

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.08 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/08-Palasai-et-al.pdf)]

Identification of genes involved in flowering in *Stevia rebaudiana* using expressed sequenc

Amin Razali, Nurul Hidayah Samsulrizal, Zarina Zainuddin

APJMBB 28 (2): 105-112

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.09 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/09-Razali-et-al.pdf)]

Phytochemical analysis of ionic liquid-Graviola (*Annona muricata*) fruit extract and its acute

Djabir Daddiouaissa, Azura Amid, Syahida Ahmad, Ahmed A. M. Elnour

APJMBB 28 (2): 113-124

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.2.10 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_2/10-Daddiouaissa-et-al.pdf)]

(/)

Volume 28 (3); 2020

Anti-inflammatory potential of the aqueous extract of *Cyamopsis tetragonoloba* against the albino rats

Jerine Peter Simon, Ram Kumar Katturaja, Arunraj Namachivayan, Sangeetha Nithyanandham, M

APJMBB 28 (3): 1-12

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.01 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/01-Simon-et-al.pdf)]

Chromatographic separations and characterization of bioactive secondary metabolites of *A* fungal strain

Amina Bramki, Edwin de Pauw, Meriem Frahtia, Andrea McCann, Gabriel Mazzucchelli, Laid Dehi

APJMBB 28 (3): 13-21

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.02 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/02-Bramki-et-al.pdf)]

K-ras peptide mimotope induces a humoral immune response against G12V K-ras antigen i stages

Winfrey Pui Yee Hoo, Pui Yan Siak, Nur Aqlili Riana Alias, Jia Jia Wong, Ee Wern Tan, Adelene Ai-Aun In

APJMBB 28 (3): 22-35

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.03 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/03-Hoo-et-al.pdf)] [Supplem (/images/publication/volume_28/issue_3/Supplemental_Hoo-et-al.pdf)]

Diabetic wound infection: A review on microbial population and infection control

Nur Amiera Syuhada Rozman, Woei Yenn Tong, Chean Ring Leong, Wen-Nee Tan, Syarifah Ab R

APJMBB 28 (3): 36-43

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.04 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/04-Rozman-et-al.pdf)]

Enhancement of very high gravity bioethanol production via fed-batch fermentation using s

Nur Adila Muradi, Dayang Salwani Awang Adeni, Nurashikin Suhaili

APJMBB 28 (3): 44-51

(/)

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.05 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/05-Muradi-et-al.pdf)]

Antibiotic resistance of ESKAPE bacteria in acute pharyngitis patients from private clinics i

Christina Shook Cheng Chong, Zhuang Mian Bo, Wei Keat Tan, Seshatharran Parmasivam, Shu T
Christopher Kwong Chong Lee, Renee Lay Hong Lim, Crystale Siew Ying Lim

APJMBB 28 (3): 52-58

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.06 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/06-Chong-et-al.pdf)] [Supple
(/images/publication/volume_28/issue_3/Supplemental_Chong-et-al_1.pdf)]

Analyses of yield related agronomic traits of Malaysian rice varieties

Nur Aini Mohd Kasim, Chui-Yao Teh, Parameswari Namasivayam, Nur Fatihah Mohd. Yusoff, Chai

APJMBB 28 (3): 59-74

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.07 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/07-Mohd-Kasim-et-al.pdf)] [S
(/images/publication/volume_28/issue_3/Supplemental_MKasim-et-al_1.pdf)] [Supplemental Data
(/images/publication/volume_28/issue_3/Supplemental_MKasim-et-al_2.pdf)]

Trihoney improves testicular weight change and histopathological alterations in hyperchole

Zenab B. Hamad Mohamed, Hamad Abdulsalam Hamad Alfarisi, Azantee Yazmie Abdul Wahab, A
Mohamad, Muhammad Bin Ibrahim

APJMBB 28 (3): 75-87

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.08 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/08-Mohamed-et-al.pdf)]

The anticancer molecular mechanism of Carnosol in human cervical cancer cells: An *in vitr*

Rand R. Hafidh, Ahmed S. Abdulamir

APJMBB 28 (3): 88-98

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.09 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/09-Hafidh-et-al.pdf)]

Method for purification of collagen: A systematic review

Nursyahidatul Azwa Awang, Azura Amid, Zatul Iffah Arshad

(/)

APJMBB 28 (3): 99-112

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.10 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/10-Awang-et-al.pdf)]

The influence of metal on the performance of 2,4,5-triphenylimidazole as an inhibitor of den

Sri Sumarsih, Muthia Dewi Pratiwi, Indah Nur Ainni, Hardinata Rachmad Sinatriya, Soegeng Soegi Setyawati

APJMBB 28 (3): 113-121

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.3.11 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_3/11-Sumarsih-et-al.pdf)]

Volume 28 (4); 2020

Anthocyanin-loaded polymeric dextran nanoparticle as an anti-proliferative agent on humar

Siti Zubaidah Abdullah, Chean Ring Leong, Woei Yenn Tong, Jyh Chyang Pang, Wen-Nee Tan, Sy

APJMBB 28 (4): 1-10

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.01 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/01-Abdullah-et-al.pdf)]

Effects of double emulsification on *Lactobacillus plantarum* NBRC 3070 stability and physic during storage

Safiah Sabrina Hassan, Intan Nabihah Ahmad Fadzil, Hifa Nazirah Mohammed Yazid, Anida Yuso

APJMBB 28 (4): 11-25

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.02 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/02-Hassan-et-al.pdf)]

Expression and characterization of family 40 Carbohydrate Binding Module (CBM) from *Vibr*

Gogula Selvi Asang, Shadariah Mamat, Nadiawati Alias, Asmad Kari

APJMBB 28 (4): 26-38

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.03 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/03-Asang-et-al.pdf)]

Effect of storage and frying times on stability of acrylamide and 5-hydroxymethylfurfural in

(/)

Rasyiqah Ridzal, Norfahana Abd-Talib, Emmy Liza Anak Yaji, Kelly Yong Tau Len, Nadia Razali, K

APJMBB 28 (4): 39-50

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.04 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/04-Ridzal-et-al.pdf)]

***In silico* molecular modelling and docking of allicin, epigallocatechin-3-gallate and gingerol**

Asita Elengoe, Elina Sebestian

APJMBB 28 (4): 51-67

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.05 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/05-Elengoe-et-al.pdf)] [Supp
(/images/publication/volume_28/issue_4/Supplemental_Elengoe-et-al.pdf)]

Bioremoval of Acephate by biofilm-forming *Enterobacter cloacae* – VITDAJ8 in a vertical pa

Dipti Mayee Dash, Ankita Itusha, Jabez Osborne W

APJMBB 28 (4): 68-80

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.06 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/06-Dash-et-al.pdf)]

Heavy metal phytoremediation: Potential and advancement

Pushpa Chaudhary Tomar, Shilpa Samir Chapadgaonkar, Varsha Panchal, Arpita Ghosh

APJMBB 28 (4): 81-93

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.07 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/07-Tomar-et-al.pdf)]

***MTHFR* rs1801133 polymorphism in Bangladeshi population – its prevalence and detection**

Sumaiya Farah Khan, Mahmuda Akter, Shayan Shahriar, MD Amzad Hossain, Abu Ashfaqur Sajib

APJMBB 28 (4): 94-101

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.08 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/08-Khan-et-al.pdf)]

Antigenic outer membrane proteins prediction of *Pasteurella multocida* serotype B:2

Farahani Muhammad Azam, Mohd. Zamri Saad, Raha Abdul Rahim, Pramote Chumnanpoen, Tee

(/)

APJMBB 28 (4): 102-116

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.09 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/09-Muhammad-Azam-et-al.p
(/images/publication/volume_28/issue_4/Supplemental_Muhammad-Azam-et-al.pdf)]

Effects of maltodextrin concentration and inlet temperature on the physicochemical propert

Yu Von Germaine Chng, Lee Sin Chang, Liew Phing Pui

APJMBB 28 (4): 117-131

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.10 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/10-Chng-et-al.pdf)]

Pre-treatment effects against the diclofenac-induced toxicity by the aqueous leaf extract of albino rats for 10 and 15 days

Jerine Peter Simon, Sibi Karthik Saravanan, Jayashree Sathiyanarayanan, Radhakrishnan Vidya,

APJMBB 28 (4): 132-143

Article DOI: https://doi.org/10.35118/apjmbb.2020.028.4.11 (https://doi.org/10.35118/apjmbb.2020.

Click here to download [PDF (/images/publication/volume_28/issue_4/11-Simon-et-al.pdf)]

About MSMBB

We are a non-profit organisation that was established in 1988 to promote molecular biology and biotechnology.

Stay Connected on:

Next Event

4th International Conference on Molecular Biology & Biotechnology

in conjunction with the 27th Scientific Meeting of the Malaysian Society of Molecular Biology & Biotechnology (MSMBB)

Beyond 2021: Building Sustainable Science

1-3rd June2021

Online Conference

Quick Links

› General Info (/index.php/about/info)
› Publication (/index.php/publication)
› Membership Subscription (/index.php/memberships/subscription)
› Membership Benefits (/index.php/memberships/benefits)
› Mode Of Payment (/index.php/memberships/payment)
› Executive Members (/index.php/about/executive-members)
› Past Presidents (/index.php/about/past-presidents)

Contacts Us

For general information about MSMBB, including registration, please contact us at:

Department of Parasitology,
Faculty of Medicine,
University of Malaya,
50603 Kuala Lumpur,
Malaysia.
the.msmbb.office@gmail.com (mailto:the.msmbb.office@gmail.com)
+603 - 7967 4744
+603 - 7967 4749

Editorial Board

Editorial Board Member

Oi Ming Lai, PhD

Lai Oi Ming is a Professor in Enzyme Technology from the Department of Bioprocess Technology, Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia. She is also a Research Fellow at the Institute of Bioscience, UPM. She is the coeditor of Healthful Lipids (AOCS Press) and lead editor of Palm Oil: Production, Processing, Characterization, and Uses (AOCS Press) book, author or co-author of more than 170 referenced SCI publications, more than 10 book chapters and the holder of 16 patents. Oi-Ming's research program includes the development and improvement of structured lipids such as diacylglycerols (DAG), medium- and long-chain triacylgycerols (MLCT), product diversification of various phytonutrients and oilseed by-products, nutraceuticals and cosmeceuticals development. She has led numerous research projects, completed two Technofund projects from MOSTI worth USD 2.5 million and completed the building of a fully operational coenzyme Q10 production plant (API at 99% purity) and has commercialized two of technologies including the recent RemdiiTM Sensitive, targeting very dry and inflamed skin conditions. In 2008, she won WIPO's (World Intellectual Property Organization) Best invention by Woman Award and was the recipient of the Top Research Scientists of Malaysia award from the Academy of Sciences, Malaysia in 2012. She also sits on the Editorial Board of the Food and Bioprocess Technology Journal, Peer J, Planters, Pertanika Journal of Scholarly reviews and others. Her h index is 24 as of 1 March 2017. She is a Guest Professor at the Department of Food Science and Engineering, Jinan University, China. She is a member of the UPM's Intellectual Property Evaluation Committee, under the purview of the Putra Science Park and also serves as a committee member of the Research Working Committee on Intellectual Property Protection and Licensing. She is also on the Executive Council panel of Experts for Malaysian Laboratories for Academia-Business Collaboration (MyLAB).

Wen Siang Tan, PhD

Wen Siang TAN is a professor of molecular virology at Universiti Putra Malaysia. He did his PhD at the University of Edinburgh under the supervision of Prof. Sir Kenneth Murray, who developed the first effective recombinant vaccine against hepatitis B virus. Wen Siang is an enthusiast of phage display and virus-like particles as well as their practical uses in the development of multi-component vaccines, drug delivery systems and immunological reagents. He loves to share his findings and inventions with scientific communities, so far he has published over 140 papers in leading scientific journals. He is one of the inventors for 17 patents and 3 trademarks have been registered under his name. He had completed the supervision of 25 PhD and 35 MSc students. In 2005, he was awarded the Norken Stiftung Research Fellowship to study structural biology in the laboratory of Prof. Malcolm Walkinshaw. In 2012, he was awarded the Top Research Scientists of Malaysia by the Academy of Sciences Malaysia.

Bambang Purwantara, DVM, MSc, PhD

Prof Purwantara is currently a full professor at the Department of Clinic, Reproduction and Pathology, Faculty of Veterinary Medicine, Bogor Agricultural University, Bogor Indonesia. He actively involved in the advisory boards of master and doctorate degrees in a number of universities. Beside his current position as the Director of Indonesian Biotechnology Information Centre (IndoBIC), Prof Purwantara was former Director of SEAMEO BIOTROP, a leading Southeast Asian Regional Centre for Tropical Biology. He is currently also President of the Indonesian Society for Agricultural Biotechnology (ISAB/PBPI), President of the Indonesian Association for Animal Reproduction (IAAR/ARHI), member of Biosafety Commission for Genetically Engineered Products (KKH PRG), member of National Expert Working Group on Food Security – Indonesian Food Security Council (Pokja Ahli DKP) 2014-2017. Prof Purwantara currently is the Director of Centre for Collaborative Research on Animal Biotechnology and Coral Reef Fisheries (CCR ANBIOCORE) IPB operated under USAID SHERA Project, partnering seven Indonesian and two US universities.
Prof Bambang Purwantara has long been working on the area of animal reproduction with special interest on reproductive biotechnology particularly in large ruminants. He has been developing basic and applied researches on sperm physiology and preservation of the bovine, sheep, goat and horses.

Fook Tim Chew, PhD

Dr Chew Fook Tim is the Vice Dean of the Faculty of Science at the National University of Singapore (NUS), taking care of the Undergraduate Programmes and Student Life sections, and an Associate Professor of the Department of Biological Sciences, NUS, teaching Epidemiology, Genetics and Immunology. He is an Editorial Board Member of several key scientific journals such as the Journal of Physiological Anthropology, Frontiers in Plant Science, Frontiers in Bioengineering and Biotechnology, and has published more than 150 major international scientific publications, holds several patents, and presented at more than 300 international and regional conferences, with more than 150 invited talks, particularly in the areas of allergies, public health, genetics and plant breeding. He is a Governing Board Member of the Southeast Asian Regional Center for Graduate Study and Research in Agriculture (SEARCA), Governing Board Member of the Southeast Asian Ministry of Education Centre for BioTropical Research (Biotrop), Chairman of the Academic Advisory Board for the School of Life Sciences at the Management Development Institute of Singapore (MDIS), Board Member of Operation Hope Foundation, and Consultant & Scientific Advisor to Several Major Agribusiness and Biomedical Companies, including Sime Darby, Olam International, First Resources, etc.

Teruna J. Siahaan, PhD

Dr. Teruna J. Siahaan is the Aya & Takeru Higuchi Distinguished Professor of Pharmaceutical Chemistry at The University of Kansas (KU) and a Fellow of the American Association of Pharmaceutical Scientists (AAPS). His research is focused on improving drug delivery to the brain and immune cells; he published 200 papers, obtained 12 patents, and edited two books. He serves as the Director of Global Health Education & Research Center, School of Pharmacy, KU; Co-Program Director of the T32 NIH Biotechnology Training Program, KU; and the Executive Board of Directors the Globalization Pharmaceutics Education Network (GPEN) Organization. He has received several honors and awards, including Self Faculty Scholar, KU; Pfizer Research Scholar Award; 2013 Mentor of the Year, KU; and 2014 PhRMA Foundation Award for Excellence in Pharmaceutics.

Mohd Ali Hassan, PhD

Professor Mohd Ali Hassan obtained his degree in Chemical Engineering at The University of Leeds, United Kingdom and PhD in Environmental Biotechnology from University of Okayama, Japan. He has more than 30 years of teaching and research experience. In 2002 he was promoted to the post of Professor at University Putra Malaysia (UPM) in the field of Environmental Biotechnology. He has worked extensively on international biomass, bioenergy and zero-emission projects throughout his career, particularly with Japan and Korea, in collaboration with the palm oil industry in Malaysia. He has succeeded in obtaining R&D funding from local and international agencies and companies. He managed to set up the Serdang Biomass Town and Biorefinery in UPM campus, since 2012. He heads an international SATREPS project on biomass and zero emission project at the palm oil mill funded by JICA-JST (Japan) and Ministry of Higher Education Malaysia. He was Dean, Faculty of Biotechnology, UPM from 2007-2014. Now he heads the Industry and Community Relations Unit at The Faculty of Biotechnology and Biomolecular Sciences UPM. He has published more than 180 journal papers, has several patents, book chapters, national and international awards. He has completed 10 research projects, with 2 commercialised products, and has supervised and graduated many postgraduate and undergraduate students. He was awarded the Top Research Scientist of Malaysia by the Academy of Sciences Malaysia in 2013, and Fellow of the Academy of Sciences Malaysia in 2016. He has also received the Research Exchange Award from the Korean Society for Biotechnology and Bioengineering, the Malaysia Research Star Award 2017 and the Malaysian Microbiology Award 2017. Currently he is Vice President of Asia Federation of Biotechnology, President of Asia Federation of Biotechnology Malaysia Chapter and a Committee Member of Biomass Asia Association. His current h index (Scopus) is 31, with more than 3000 citations.

Margaret Duffy, PhD

Margaret Duffy is a Research Fellow of the Kay Kendall Leukaemia Fund, pursuing research into haematological malignancies with a focus on multiple myeloma. Margaret achieved a 1st class honours degree in Biomedical Science from the National University of Ireland Galway, before completing a PhD at the University of Glasgow. Her PhD studies centred around viral:host interactions and improving the stability of adenoviral vectors in blood. Her subsequent postdoctoral research was focused on developing adenoviruses as tools for gene therapy, vaccination and oncolytic applications. Margaret also spent time working as a Marie Curie IAPP researcher at a biotech company in the Netherlands, specialising in adenovirus vectorisation and production. Now based at the Department of Oncology University of Oxford, her research is based on developing new oncolytic viruses for blood cancers.

List of Associate Editors

Associate Editor	Field of interests
MS Kanthimathi, PhD (UM, Malaysia)	Natural products, Antioxidants, Free radicals, Biochemistry
Lionel In Lian Aun, PhD (UCSI University, Malaysia)	Molecular Oncology, Cancer Immunology, Immunotherapeutics, Molecular Biology
Wang Seok Mui, PhD (UiTM, Malaysia)	Virology, Molecular Diagnostics
Amirah Amir, PhD (UM, Malaysia)	Medical parasitology, Malaria, Malaria culture, Anopheles colonization

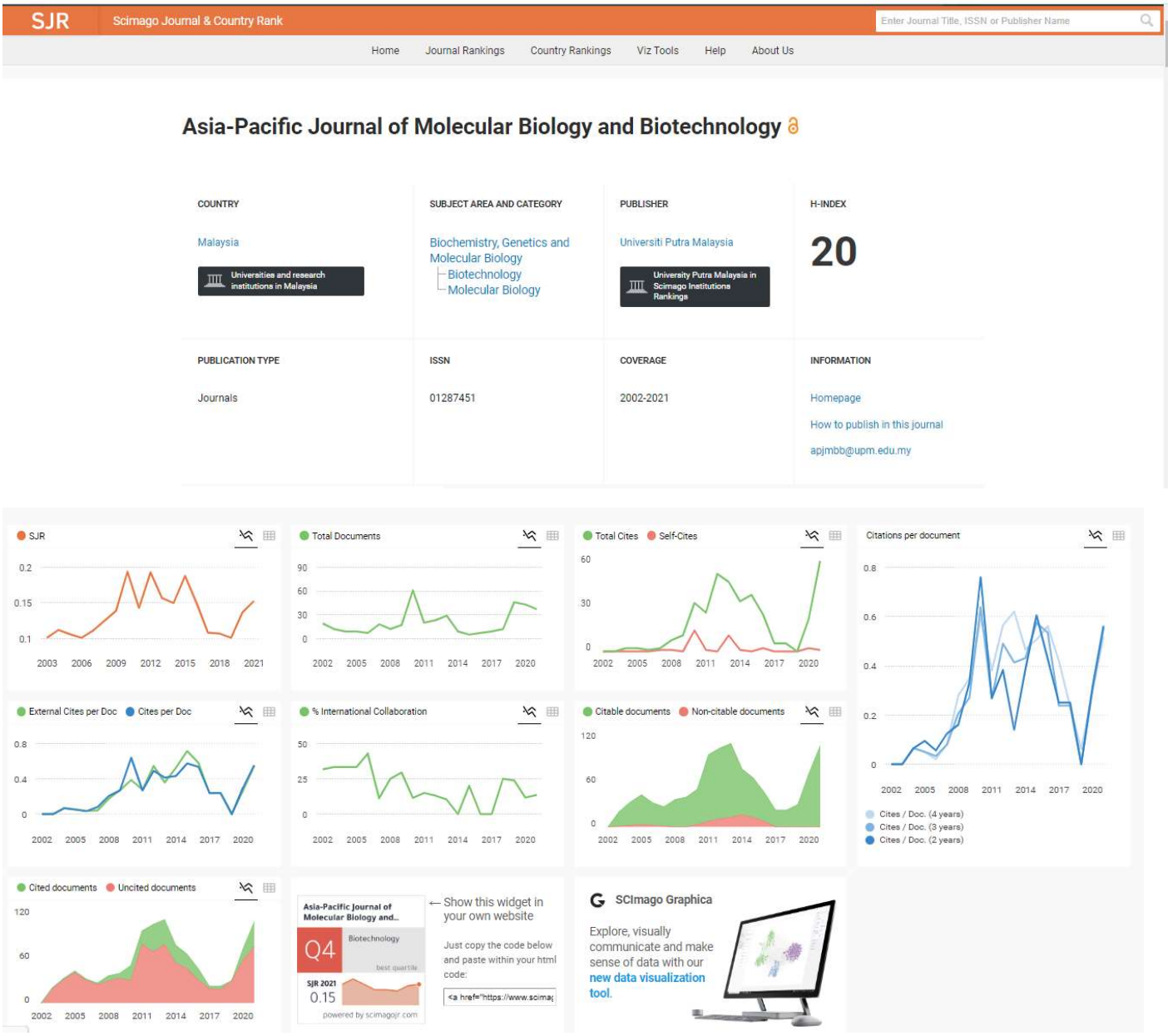
Tang Thean Hock, PhD (USM, Malaysia)	RNA-Biology, Nucleic Acid Aptamer, Mol. Diagnostic
Siti Sarah Othman, PhD (UPM, Malaysia)	Infection & Immunity, Bacterial pathogenesis, Microbiology, Molecular Biology
Crystale Lim Siew Ying, PhD (UCSI University, Malaysia)	Gene expression, Host-pathogen Interaction, Antibiotic Resistance, Tumorigenesis
Boon Chin Tan, PhD (UM, Malaysia)	Plant Molecular Biology, Proteomics, Metabolic Engineering
Wan Nur Ismah Wan Ahmad Kamil, PhD (UPM, Malaysia)	Bacteriology, Pathogenicity, WGS
Lau Yee Ling, PhD (UM, Malaysia)	Malaria, Molecular Parasitology
Mas Jaffri Masarrudin, PhD (UPM, Malaysia)	Nanobiotechnology, Drug Delivery, Anticancer Therapeutics, Microbial-synthesis of Nanomaterials
Adelene Song Ai Lian, PhD (UPM, Malaysia)	Molecular Biology, Metabolic Engineering, Lactic Acid Bacteria, Microbial Cell Factory
Saila Ismail, PhD (UPM, Malaysia)	Microbiology, Virology, Immunology

Cheong Fei Wen, PhD (UM, Malaysia)	Proteomics and Vector Borne Diseases (Malaria)
Irwan Hanish Warsanah, PhD (UPM, Malaysia)	Microbiology, Immunology
Jeremy Ryan de Silva, PhD (UM, Malaysia)	Medical Parasitology, Clinical Microbiology, Immunology
Mohd Termizi Yusof, PhD (UPM, Malaysia)	Biological Sciences, Mycology
Siti Aminah Ahmed, PhD (USM, Malaysia)	Molecular Biology, Diagnostic Kits, RNA-seq
Tan Yee Shin, PhD (UM, Malaysia)	Mycology
Wong Pooi Fong, PhD (UM, Malaysia)	Genomic, Molecular Pharmacology, Virology
Zetty Norhana Balia Yusof, PhD (UPM, Malaysia)	Plant Metabolism, Algae and Plant Biotechnology
Yuka Hara, PhD (INTI International University, Malaysia)	Immunology, Microbial Genomics and Molecular Biology
Ng Siew Kit, PhD (USM, Malaysia)	Antiviral Innate Immunity, A-to-I RNA Editing, Antioxidant

Citartan Marimuthu, PhD (USM, Malaysia)	Aptamers and Sensors, Non-protein coding RNA, Molecular Diagnostics
Siti Hawa Ngalim, PhD (USM, Malaysia)	Cell Migration, MSC, Nanobiotech
Chinni Venkata Suresh Babu, PhD (AIMST University, Malaysia)	Transcriptome, ncRNA, Bioinformatics
Hazrina Yusof, PhD (USM, Malaysia)	Bioinformatics
Ronald Teow, PhD (Sunway University, Malaysia)	Biomarker, Epigenetics, Microbiome, Cancer
Tye Gee Jun, PhD (USM, Malaysia)	Immunology, Vaccine Development, Mammalian Cell Expression
Pui Liew Phing, PhD (UCSI University, Malaysia)	Food Biotechnology
Michelle Soo, PhD (UCSI University, Malaysia)	Systematics and Taxonomy Research
Bimo Tejo, PhD (UPM, Malaysia)	Biochemistry, Biotechnology, In silico Protein Structure, Peptidomimetics
Lee Sau Har, PhD (Taylor's University, Malaysia)	Cancer Stem Cell Biology, Cancer Biology, Virology, Traditional Medicine and Natural Products

Sobia Manzoor, PhD (NUST, Pakistan)	Medical, Virology
Kenny Voon, PhD (IMU, Malaysia)	Medical, Virology
Khor Goot Heah, PhD (UiTM, Malaysia)	Oral Sciences, Molecular Biology, Cancer Biology, Histochemistry, Oral Pathology, Microarray, Gene Expression, Epigenetic Studies, Natural Products
Umaiyal Munuswamy, PhD (UPM, Malaysia)	Sustainable Agriculture, Molecular Biology, Biotechnology, Genetics, Proteomics, Metabolomics, Transcriptomics, Bioinformatics
Hann Ling Wong, PhD (UTAR, Malaysia)	Plant-Microbe Interaction, Plant Biotechnology, Molecular Biology, Synthetic Biology

BUKTI SCOPUS



BUKTI KORESPONDENSI

Submitting my manuscript Inbox ×

harsasi setyawati <harsasi-s@fst.unair.ac.id> Sat, Apr 11, 2020, 6:28 PM
to apjmbb

Dear Dr. Chia Suet Lin, Managing Editor of APJMBB ,
Herein with this email, I send you my manuscript and my cover letter to be considered published in APJMBB. Hopefully, my manuscript could be reviewed and published.

Thank you for your attention.
--
Kindest regard,
Harsasi Setyawati, S.Si., M.Si
Department Chemistry
Faculty of Science and Technology
Universitas Airlangga

2 Attachments • Scanned by Gmail

Re-submitting manuscript Harsasi Setyawati Inbox ×

harsasi setyawati <harsasi-s@fst.unair.ac.id> Sun, May 17, 2020, 5:04 PM
to ASIA

Dear Dr. Chia Suet Lin, Managing Editor of APJMBB ,
Herein with this email, I send you my revised-manuscript, my cover letter, and my responses to the reviewer. I have revised my manuscript according to suggestion of all reviewers. Hopefully, my manuscript could be considered published in APJMBB.
Thank you.

--
Kindest regard,
Harsasi Setyawati, S.Si., M.Si
Department Chemistry
Faculty of Science and Technology
Universitas Airlangga

3 Attachments • Scanned by Gmail

BUKTI KORESPONDENSI

REVISION MANUSCRIPT HARSASI SETYAWATI Inbox ×

harsasi setyawati <harsasi-s@fst.unair.ac.id> Sun, Jul 5, 2020, 4:24 PM
to ASIA

Dear Dr. Chia Suet Lin, Managing Editor of APJMBB,
Herein with this email, I send you my revised-manuscript, my responses to the reviewer also the English editing certificate. I have revised my manuscript according to suggestion of all reviewers. Hopefully, my manuscript could be considered published in APJMBB.
Thank you.

--
Kindest regard,
Harsasi Setyawati, S.Si., M.Si
Department Chemistry
Faculty of Science and Technology
Universitas Airlangga

3 Attachments • Scanned by Gmail

3_REVISION MANUSCRIPT HARSASI SETYAWATI Inbox ×

harsasi setyawati <harsasi-s@fst.unair.ac.id> Thu, Aug 6, 2020, 9:07 AM
to ASIA, TEGUH, teguhharisucipto

Dear Dr. Chia Suet Lin, Managing Editor of APJMBB,
Herein with this email, I send you my revised-manuscript and my responses to the reviewer's comment. I have revised my manuscript according to the suggestion of all reviewers. Hopefully, my manuscript could be considered published in APJMBB.
Thank you.

--
Kindest regard,
Harsasi Setyawati, S.Si., M.Si
Department Chemistry
Faculty of Science and Technology
Universitas Airlangga

2 Attachments • Scanned by Gmail

BUKTI KORESPONDENSI

Re-payment publication fee of Harsasi Setyawati

harsasi setyawati <harsasi-s@fst.unair.ac.id> Wed, Aug 26, 2020, 7:17 PM
to ASIA

Dear Editor,
Herein with this email I send you the evidence of my re-payment for publication fee. Hopefully this payment is not rejected again.

Thank you
Kindest regards,
Harsasi Setyawati

One attachment • Scanned by Gmail

FINAL_REVISION MANUSCRIPT HARSASI SETYAWATI Inbox ×

harsasi setyawati <harsasi-s@fst.unair.ac.id> Thu, Aug 13, 2020, 8:35 PM
to ASIA, TEGUH

Dear Dr. Chia Suet Lin, Managing Editor of APJMBB,
Herein with this email, I send you :
1. My final revised-manuscript
2. My responses to the editor comments
3. All figures in JPEG format
4. Excel for Figure 5,6,7
5. Proof payment of APC

I have revised my manuscript according to the suggestion of Editor in Charge. Hopefully, my manuscript could be considered published in APJMBB.
Thank you.

--
Kindest regard,
Harsasi Setyawati, S.Si., M.Si
Department Chemistry

BUKTI KORESPONDENSI

FINAL_REVISION REFERENCE FORMAT Inbox ×

harsasi setyawati <harsasi-s@fst.unair.ac.id> Thu, Aug 27, 2020, 12:44 PM
to ASIA

Dear Dr. Chia Suet Lin, Managing Editor of APJMBB,
Herein with this email, I send you the revision reference format of my manuscript.
Thank you

--
Kindest regard,
Harsasi Setyawati, S.Si., M.Si
Department Chemistry
Faculty of Science and Technology
Universitas Airlangga

One attachment • Scanned by Gmail

Comment for Proofreading Manuscript Sumarsih et al Inbox ×

harsasi setyawati <harsasi-s@fst.unair.ac.id> Sat, Sep 5, 2020, 7:23 PM
to ASIA

Dear editor APJMBB,
After checking my manuscript, I notice **only one mistake in the reference** :
In the manuscript written " Setiati "
The correct is E Setiati. In this manuscript, the "E" letter is gone.

I also have put my comment on the pdf file.

Thank you

--
Kindest regard,
Harsasi Setyawati, S.Si., M.Si
Department Chemistry
Faculty of Science and Technology
Universitas Airlangga

AsPac J. Mol. Biol. Biotechnol. 2020
Vol. 28 (3) : 113-121

The influence of metal on the performance of 2,4,5-triphenylimidazole as an inhibitor of dengue virus replication

Sri Sumarsih[a], Muthia Dewi Pratiwi[a], Indah Nur Ainni[a], Hardinata Rachmad Sinatriya[a], Soegeng Soegijanto[b], Teguh Hari Sucipto[b], Harsasi Setyawati[a*]

[a]*Department of Chemistry, Faculty of Science and Technology, Airlangga University, Surabaya 60119, Indonesia*
[b]*Dengue Study Group, Institute of Tropical Disease, Airlangga University, Kampus C Jl. Mulyorejo, Surabaya, East Java, Indonesia, 60115*

Received 12th April 2020 / Accepted 6th August 2020

Abstract. Dengue is a contagious disease caused by dengue virus and transmitted to humans by the bite of infected *Aedes aegypti* mosquito. Imidazole and its derivatives are proven have ability impairing dengue virus. One of potential imodazole's derivatives is 2,4,5-triphenylimidazole (TPI). The presence of metal to the 2,4,5-triphenylimidazole (TPI) structure through a complex compound formation highly contributes to their ability as an inhibtor dengue virus replication. Iron, cobalt and zinc were used as an ion center in the complex compound. Complex Zn-TPI and Fe-TPI showed low cytotoxic effect at all the evaluated concentrations (viability > 50%). Complex Co-TPI showed reduction of DENV-3 growth, at the lowest concentration (6.25 μg/ml) exhibited the antiviral activity (DENV-3 reduction 43%). For Fe-TPI and Zn-TPI, the reduction values of DENV-3 were 56% and 54.9% respectively.

Keywords: metal, 2,4,5-triphenylimidazole, influence, complex-compound, inhibitor, virus-replication

INTRODUCTION

Dengue is one of the most important public health problems affecting the global community. This disease commonly occurs in the tropic and sub-tropics area, and Indonesia becomes one of the countries that has the largest dengue-endemic region (E Setiati *et al.,* 2006; Fahri *et al*., 2013; Kotaki *et al*., 2014). Until now, there is no vaccine or anti-viral for humans that could overcome this disease. Imidazole and their derivatives are proven has potency against dengue virus infection in cell lines (Sucipto *et al*., 2018; Sucipto *et al*., 2017). On the other hand, the presence of metal on the structure of organic ligand is proven could improve their biological activity (Geersing *et al.,* 2018) The complex compound is formed as a result of metal and organic compound reaction. It can be used as an anti-inflammatory, antimicrobial, antifungal, antibacterial, and antivirus (Agotegaray *et al*., 2012; Arjmand, Mohani, & Ahmad, 2005; Ranford, Sadler, & Tocher, 1993). The metal complexes with deprotonated imidazole as ligand hold promise as an approach to enhance the biological activity. Previous reports have described the use of cobalt(II)-morin and zinc(II)-morin based systems for anti-DENV (dengue serotype) type 2 applications. The value of inhibition activity of zinc(II)-morin was 2.00 μg/ml and cobalt(II)-morin was 3.08 μg/ml (Sucipto *et al*., 2017; Sucipto *et al*., 2019).

Thus, this research investigated the influence of metals on the imidazole derivative (2,4,5-triphenylimidazole) in their anti-dengue activity. Studies on the compound of imidazole-4,5- showed higher antiviral potency against yellow fever virus (YFV) than dengue virus (DENV).

*Author for correspondence: Harsasi Setyawati, Department of Chemistry, Faculty of Science and Technology, Airlangga University, Surabaya 60119, Indonesia. Email – harsasi-s@fst.unair.ac.id

This bioactivity may be within the imidazole series of a 'para-'attachment of a heterocycle to its 'C' (Saudi *et al.*, 2014).This research only focuses on Iron(II), Cobalt(II) and Zinc(II) as metal resources because three of them exhibit biological activity for humans and include as an essential mineral that needed by the humans body. The interaction of metals and 2,4,5-triphenylimidazole as a ligand was investigated through to the complex compound formation and characterized by spectrophotometer UV-Vis, spectrophotometer FTIR, and electron microscope. An inhibitor virus assay will be investigated through the ELISA (Enzyme-Linked Immunosorbent Assay) method using dengue virus type 3.

MATERIALS AND METHODS

Materials

Materials used were pure analysis (pa) degree. They were 2,4,5-triphenylimidazole (TPI), zinc chloride ($ZnCl_2$), cobalt (II) chloride di hydrate ($CoCl_2.2H_2O$), iron (III) chloride hexahydrate ($FeCl_3.6H_2O$), N, N-dimethyl formamide (DMF), methanol, ethanol 95%, distilled water, Vero cells derived from the kidney of an African green monkey from ATCC, Dimethyl Sulfoxide (DMSO) (Merck 99,98%), Minimum Essential Medium Eagle (MEM) Media (Sigma-Aldrich), Fetal Bovine Serum (Biowest), L-glutamine, $NaHCO_3$, Trypsin-EDTA, Dengue virus type 3 (DENV-3) Surabaya Isolate with GenBank accession number KF709426, Cell Proliferation Reagent WST-1 (Roche Applied Science), counting cells and DENV antibody (4G2) for Enzyme-Linked Immunosorbent Assay (ELISA).

Synthesis and characterization of complex compounds from metal and 2,4,5-triphenylimidazole as a ligand

All of the complex compounds were synthesized with the ratio mole metal to ligand = 1:1 (Martak *et al.,* 2016; Sucipto & Martak, 2016). The metal was dissolved by ethanol and reacted to the ligand (in ethanol) and then put in a 25 ml flask and then refluxed for 4 hours at 76°C. After that, the mixture was left until the sediment formed. Next, the sediment was separated from the filtrate then washed with 5 ml of ethanol then dried in a desiccator (Martak *et al.*, 2016). All of solids were characterized by Olympus light microscope, spectrophotometer UV-VIS and spectrophotometer FTIR.

Vero cells preparation

Vero cell lines (African green monkey kidney) was used in this study, maintained and propagated in Minimum Essential Eagle Medium containing 10% fetal bovine serum. Cultured Vero cell lines were incubated at 37°C, respectively in 5% CO_2. Confluent monolayer of Vero cells were detached with trypsin-EDTA and incubate cells at 37°C for 5 minutes. Then Minimum Essential Eagle Medium containing 10% fetal bovine serum was added by pipetting gently to break up any clumps of cells and counted using a Hemocytometer. Next, cells in 96-well plate with 1×10^6 cells/10 ml were added and incubated in 37 °C incubator with 5 CO_2 cells were monitored daily until cells reached a >90 % confluent monolayer (Ammerman *et al.,* 2008; Plotkin *et al.,* 2018).

Antiviral activities assay

First, Vero cells were added with 2 ml trypsin-EDTA then incubated with 5% CO_2 at 37 °C for 5 minutes. Then, it was added with 8 ml of the new MEM 10% FBS and was vortexed until it was homogenous. After that, 10 µl was pipetted and added with tryptophan blue strain. Then, the living cell was counted by a Hemocytometer counting chamber. This process required Vero cells ($1x10^6$ cells/10ml) in a 96-well plate (Ammerman *et al.*, 2008).

Second, preparation of a complex compound (each complex compound) was weighed 0.0006 gram, dissolved with 4 µl DMF and added by 996 µl of MEM 10% FBS. Then, it was vortexed until homogeneous. After being homogeneous, 150 µl of the complex compound was added in every well in U bottom plate and then added by 50 µl MEM 10% FBS to it. The first well line 50 µl was pipetted which was then filled in the second well line and so on. This process gets complex compound with various concentrations (serial dilution).

To the flat bottom plate, was added by a mixture of 50 µl of Vero cells, 25 µl of a complex compound, and 25 µl of the DENV-3 (2×10^4 FFU/well). 100 µl medium control and 100 µl of

cell control were added. Subsequently, the plates were incubated with 5% CO_2 at 37°C for 24 hours. Finally, the plate was verified using DENV antibody (4G2) for quantitative ELISA using Microplate Reader with a wavelength of 415 nm (Sucipto *et al*., 2018).

Cytotoxicity assay

First, Vero cells were added with 2 ml trypsin-EDTA then incubated with 5% CO_2 at 37°C for 5 minutes. Then, 8 ml new MEM 10% FBS was added and was vortexed until homogenous. After that, 10 µl was pipetted and added by tryptophan blue strain. Then, the living cell was counted with a Hemocytometer counting chamber. This process required Vero cells ($1x10^6$ cells/10ml) in a 96-well plate. Monitor cells until cells reach a >90 % confluent monolayer (Ammerman *et al*., 2008). Second, preparation of a complex compound (each complex compound) was weighed 0.0006 gram, dissolved with 4 µl DMF and added by 996 µl of MEM 10% FBS. Then, it was vortexed until it is homogeneous. Next, 150 µl of the complex compound was added in every well in U bottom plate and then 50 µl MEM 10% FBS was added. The first well line 50 µl was pipetted which was then filled in the second well line and so on. This process got the complex compound with various concentrations (serial dilution).

After that, a 50 µl serial dilution was added to the Vero cells that had been prepared on the first day. Then, added 50 new MEM that containing 10% FBS. Then incubated 24 hours at 37 °C. After that second day, the supernatant was removed which was then washed twice with PBS. Then 100 µl of the new MEM 10% FBS was added and added 10 µl of WST-1 reagent into Vero cells. Then the mixture was vortexed until homogeneous which is then incubated 30-60 minutes. After that, it is analyzed with a microplate reader with a wavelength of 450 nm and a reference wavelength of 650 nm (Sucipto *et al*., 2018).

Statistical analysis

Microsoft Excel 2010 for Windows was used to determine the cytotoxicity concentration 50 (CC_{50}), inhibitory concentration (IC_{50}) values of the complex compounds, *t* test and standard deviation. A *p* value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

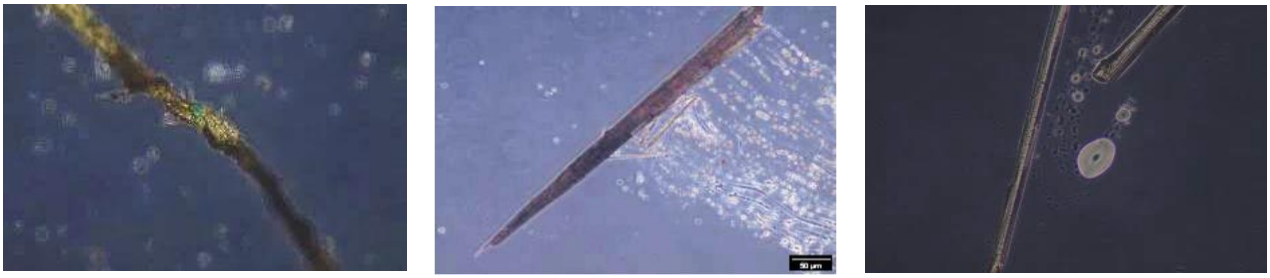
Synthesis of complex compounds

In this research, complex compounds were synthesized using the reflux method by reacting 2,4,5-triphenylimidazole (TPI) as a ligand and Fe, Co and Zn as a central atom. The complexes were synthesized using ratio mole metal to ligand 1:1. The obtained crystals were then put in the freeze dryer to make the complete dryness of crystal. The crystals that formed was characterized by light microscope (Figure 1). Complex Co-TPI and Zn-TPI showed a perfect needle crystal. However, Fe-TPI showed a broken needle crystal. The broken crystal is caused by high heating temperature when crystallization step.

Characterization of complex compounds

Complex compounds that have been successfully synthesized then characterized to determine their nature and characteristic. The characterization was conducted by UV-Vis spectrophotometer and FTIR spectrophotometer.

Characterization using UV-Vis spectrophotometer was used to determine the maximum wavelength and UV-Vis spectra pattern in a compound. The crystalline of the complex compound was dissolved with DMF, then the absorbance was measured (Figure 2 and Table 1). Figure 2 and Table 1 show that there is a shift in the maximum wavelength of the complexes and the ligand. This peak shifted due to the density of asymmetric electric charges in the imidazole ring was altered after coordinated with metal ions. It will drive a shift over a wide absorption range because the metal ion has many electrons on the d orbital. Consequently, the π- π^* transition takes place easier. All complex compounds show the maximum wavelength in the UV region (under 400 nm). This wavelength shows the metal-ligand charge transfer phenomenon which only has by complex compound (Deng *et al*., 2012).



(a) Fe-TPI (b) Co-TPI (c) Zn-TPI

Figure 1. Crystal of TPI- complex compounds. (a) for Fe-TPI complex (b) for Co-TPI (c) for Zn-TPI. Each solid has been characterized by light microscopes with 40x magnification.

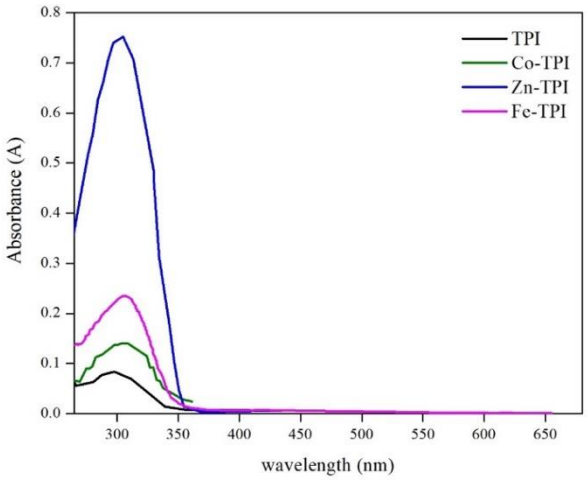


Figure 2. The electronic spectra of complex compounds on DMF solvent. All solutions were charcterized by spectrophotometer UV-VIS in the region 200-650 nm.

Table 1. The maximum wavelength of complex compounds Fe-TPI, Co-TPI, Zn-TPI, and the ligand TPI. All compounds were soluted in DMF solvent.

Compound	Maximum wavelenth (nm)
TPI	304
Fe-TPI	308.5
Co-TPI	309
Zn-TPI	306

Characterization using FTIR spectrophotometer was used to determine the functional groups formed in the complex compound and to determine the bonds formed between metals and ligands. The result of the FTIR spectra shows that there are differences in the FTIR spectra of TPI ligands and the complex compounds (Figure 3 and Table 2).

If we compare the spectra of the ligand and the complexes, we can see that there is some shifted of the wavenumber on characteristic functional group. In other words, the metal is proven bonded to the ligand structure. From this characterization we also could conclude that all metals from complex compounds have bonded to the –N- functional group from ligand. (Figure 4).

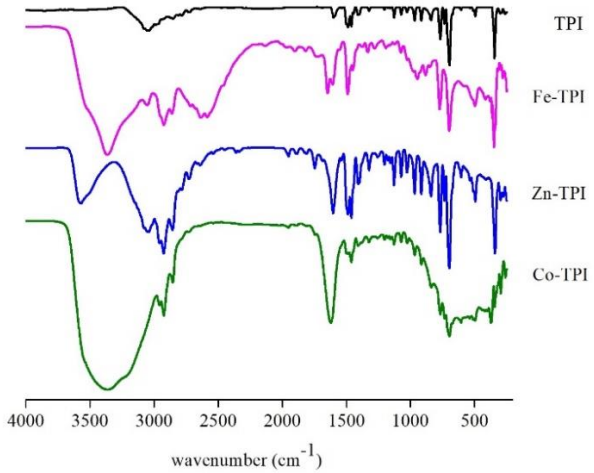


Figure 3. The FTIR spectra of complex compounds Fe-TPI, Co-TPI, Zn-TPI, and the ligand TPI. All compounds were characterized by FTIR the wavenumber range 3500-250 cm^{-1}.

Table 2. The FTIR spectra data of complex compounds Fe-TPI, Co-TPI, Zn-TPI. The spectra of complex compounds were compared with the ligand spectrum TPI.

Functional Group	Wavenumber (cm^{-1})			
	TPI	**Fe-TPI**	**Co-TPI**	**Zn-TPI**
Metal-N	-	370.33	368.4	298.96
O-H	3591.45	3365.78	3379.28	3650
N-H	3100.34	3124.21	3367.71	3113.13
C-H	2924.47	2856.58	2924.09	2988.08
C=C	1601.65	1489.05	1504.48	1602.85
C-N	1129.09	1604.77	1627.92	1128.36

Reference: (Badertscher *et al.,* 2009).

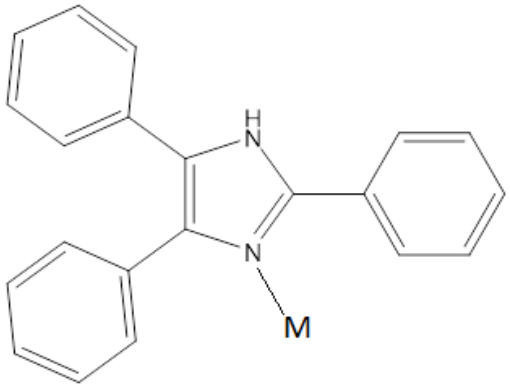


Figure 4. The bonding prediction of metal ion (M) with a functional group of TPI ligand. M is metal ion Fe, Co, and Zn that act as central ion of complex compound.

Anti-dengue activity of complex compounds. The purpose of this study is to find antiviral to DENV-2 using Vero cells line (IC_{50}). Vero cells could be infected by DENV as well as hepatocyte cells because the characteristic of the cell is similar to hepatocyte which is a host of dengue virus to replicate itself. The CC_{50} presented cytotoxicity level of complex compounds against the host, and the host used in the study was Vero cells.

Based on Table 3, all complexes have IC_{50} lower than their CC_{50} except Co-TPI. It means that almost all complexes are able to kill the pathogen before destroying the host cell. This condition is beneficial because the complex compound only kill the virus-cell without make suffering the host.

As shown in Figure 5, we can see that TPI and Cu-TPI are classified as highly toxic compared by Fe-TPI and Zn-TPI which classified as a medium toxic. The inhibition at IC_{50} was not significantly higher (p<0.005) compared to that of the metal-free imidazole (IC_{50} = 0.38 μg/ml). But, the metal-free imidazole is more toxic for Vero cells (CC_{50} = 2.91 μg/ml). The level of toxicity of an extract is classified based on the IC_{50} value, which is a very high category (highly toxic) if it is able to kill 50% of larvae at a concentration of 1-10 μg/ml, a medium category (medium toxic) at a concentration of 10-100 μg/ml and a low category (low toxic) at a concentration of 100-1000 μg/ml (Thiel *et al.,* 1982) . For this purpose, we tested each compound at various concentration and observed that both Zn-TPI and Fe-TPI low exhibit any cytotoxic effect at all the evaluated concentrations (viability > 50%). Compound Co-TPI showed reduction of DENV-3 growth, at the lowest concentration (6.25 μg/ml) exhibited the antiviral activity (DENV-3 reduction 43%). It showed reduction of DENV-3 56% and 54.9%.

In this study, medium control and cell control were treated without DENV-3. The data distribution of mean of response from each concentration was normal, with p-value more than 0.05. The response is a total energy from cell mitochondrial in each concentration of complexes. The value of response from medium control was <0.001 and value of cell control was >2.63, with analogy viability cells medium control is 0% and control cells is 100%. The data in this study was analyzed by using t-test on Microsoft Excel 2010 and inhibition of compound to DENV-3 replication was significant (p value <0.05). The Figure 6 indicates the mean of response with its standard deviation.

The C terminal in the imidazole structure plays important role to improve cellular uptake and nuclear localization of complex compound. Besides, phenyl-imidazole has a great potential as drug candidate to treatment of a variety of viral diseases, phenyl rings in imidazole presence of electron withdrawing groups improved the biological activity (Sharma *et al*., 2009).

Table 3. The anti-dengue activity of complex compounds in terms of cytotoxicity concentration.

Compound	Cytotoxicity Concentration (CC_{50}) (µg/ml)	Inhibition Concentration (IC_{50}) (µg/ml)	Selectivity Index (SI)
TPI*	36.75	1.46	25.17
Fe-TPI	1231.71	98.66	12.48
Co-TPI	509.14	-56.29	-9.04
Cu-TPI	44.17	2.30	19.20 [(Sucipto *et al.*, 2018)]

*Unpublished Data

(CC50), Inhibition Concentration (IC50), and Selectivity Index (SI). The anti-dengue activity of complex compounds was also compared with the ligand TPI.

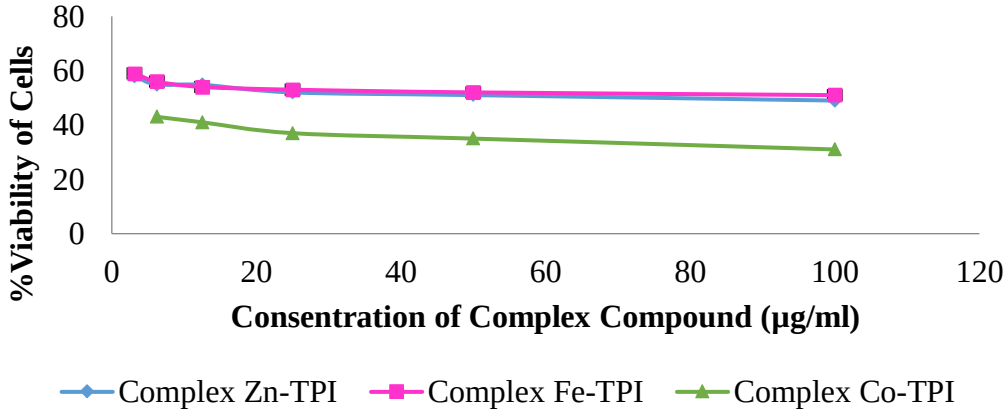


Figure 5. The inhibition DENV-3 curve of complex compounds Fe-TPI, Co-TPI, and Zn-TPI. The inhibition activity was gained by analyzing the inhibition of Vero cells that treated with the complex compounds.

In the present study, the death cell rates were not determined for the Vero cells that were treated for 24 h by the complex compound with different concentrations. The results revealed that it was found that these complex compound stimulate almost same with Vero cells compared to control (data not shown), for example in the 200 µg/ml concentration of complex compounds not showed the cell death with shown viability of cells >100% (Figure 7). This result demonstrates that three complex compounds did not cause the death cell or toxic effects on Vero cells. If the concentration of the compound is high, it will be toxic and could inhibit cell growth. A strong oxidative compound can cause cell death in more than one way: passive cell death, such as necrosis caused by the disruption of osmotic balance and apoptosis, such as active cell death caused by caspases. Based on previous research, active cell death is characterized by cytoplasmic vacuolation, largely in the endoplasmic reticulum and by the absence of caspases (cysteine proteases) (Sucipto & Martak, 2016).

Compare with a previous study, for example Cu-TPI (Sucipto & Martak, 2016), the result of cytotoxicity and antiviral activity of DENV-3 for three complex compounds in this study showed low cytotoxicity to Vero cells and high activity. Activity against human immunodeficiency virus type 1 (HIV-1) strain IIIB and HIV-2 strain ROD in MT-4 cells (IC_{50}) by Zn(II) with 3,14-dimethyl-2,6,13,17-tetraazatricyclo(16.4.0.$0^{7,12}$)docosane) diacetate ligand were 3.50 ± 0.33 µM and >110.67 µM (Biot *et al.,* 2012).

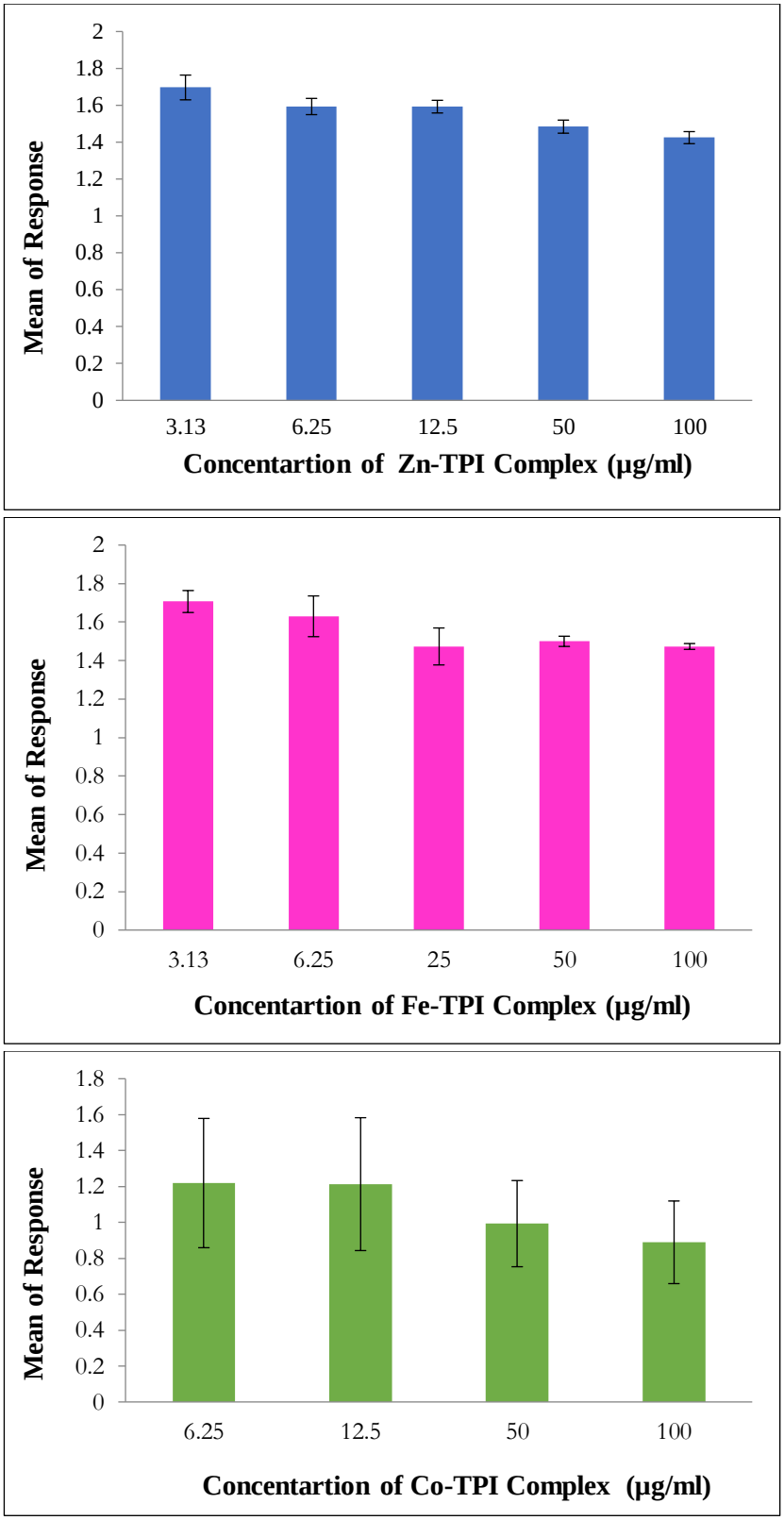


Figure 6. Standard deviation curve on the antiviral assay of complex compounds Fe-TPI, Co-TPI, and Zn-TPI. For Fe-TPI and Zn TPI complex was analyzed in 5 concentrations. However, for the Co-TPI complex, in 4 concentrations.

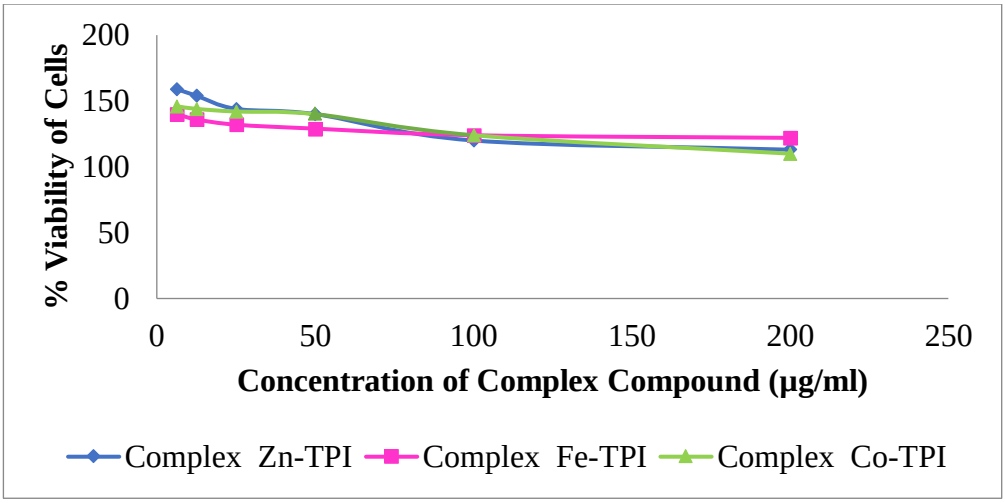


Figure 7. The cytotoxicity curve of complex compounds Fe-TPI, Co-TPI, and Zn-TPI. The cytotoxicity curve was gained by analyzing the cytotoxicity of Vero cells that treated with the complex compounds.

According to SI value, almost complex generate value more than 3. This denotes that almost complex compounds has a high selectivity. A compound is said to have high selectivity if the SI value is ≥ 3 and is said to be less selective if it has SI value <3 (Prayong *et al.,* 2008). Selectivity means that only viral cells are attacked while normal cells are not attacked (Alali *et al.,* 1999). For Co-TPI, the result shows negative on the CC_{50}, IC_{50} and Selective Index (SI). This result revealed that this complex is highly toxic so the result will always be negative

CONCLUSION

This research successfully investigated the influence of metal presence on the anti-dengue activity of derivative imidazole. The interaction of metal and 2,4,5-triphenylimidazole was revealed through the complex compound formation. All of the obtained complex compounds showed a bathochromic shift of wavelength and indicate a metal-ligand bonding through – N- group from the ligand. Complex Fe-TPI and Zn-TPI showed potency as an inhibitor of dengue viruses. However, Co-TPI complex was not found to be potent as an anti-dengue candidate.

REFERENCES

Agotegaray, M. A., Dennehy, M., Boeris, M. A., Grela, M. A., Burrow, R. A., & Quinzani, O. V. 2012. Therapeutic properties, SOD and catecholase mimetic activities of novel ternary copper (II) complexes of the anti-inflammatory drug Fenoprofen with imidazole and caffeine. *Polyhedron* 34(1): 74-83.

Alali, F. Q., Liu, X.-X., & McLaughlin, J. L. 1999. Annonaceous acetogenins: recent progress. *Journal of Natural Products* 62(3): 504-540.

Ammerman, N. C., Beier-Sexton, M., & Azad, A. F. 2008. Growth and maintenance of Vero cell lines. *Current Protocols in Microbiology* 11(1): A. 4E. 1-A. 4E. 7.

Arjmand, F., Mohani, B., & Ahmad, S. 2005. Synthesis, antibacterial, antifungal activity and interaction of CT-DNA with a new benzimidazole derived Cu (II) complex. *European Journal of Medicinal Chemistry* 40(11): 1103-1110.

Badertscher, M., Bühlmann, P., & Pretsch, E. 2009. Structure determination of organic compounds: Tables of Spectral Data: Springer.

Biot, C., Castro, W., Botté, C. Y., & Navarro, M. 2012. The therapeutic potential of metal-based antimalarial agents: implications for the mechanism of action. *Dalton Transactions* 41(21): 6335-6349.

Deng, J., Guo, L., Xiu, Q., Zhang, L., Wen, G., & Zhong, C. 2012. Two polymeric metal complexes based on polycarbazole containing complexes of 8-hydroxyquinoline with Zn (II) and Ni (II) in the backbone: Synthesis, characterization and photovoltaic applications. *Materials Chemistry and Physics* 133(1): 452-458.

E Setiati, T., FP Wagenaar, J., D de Kruif, M., TA Mairuhu, A., CM van Grop, E., & Soemantri, A. 2006. Changing epidemiology of dengue haemorrhagic fever in Indonesia.

Fahri, S., Yohan, B., Trimarsanto, H., Sayono, S., Hadisaputro, S., Dharmana, E., .Sasmono, R. T. 2013. Molecular surveillance of dengue in Semarang, Indonesia revealed the circulation of an old genotype of dengue virus serotype-1. *PLoS Neglected Tropical Dissease* 7(8): e2354.

Geersing, A., Se gaud, N., van der Wijst, M. G., Rots, M. G., & Roelfes, G. 2018. Importance of metal-ion exchange for the biological activity of coordination complexes of the

biomimetic ligand N4Py. *Inorganic Chemistry* 57(13): 7748-7756.

Kotaki, T., Yamanaka, A., Mulyatno, K. C., Churrotin, S., Labiqah, A., Sucipto, T. H., Konishi, E. 2014. Continuous dengue type 1 virus genotype shifts followed by co-circulation, clade shifts and subsequent disappearance in Surabaya, Indonesia, 2008–2013. *Infection, Genetics and Evolution* 28: 48-54.

Martak, F., Cahyani, N. W. D., Nugraheni, Z. V., & Utomo, W. P. 2016. Properties and Toxicity of Cobalt (II) Complex with 2, 4, 5-triphenyl-1H-imidazole Ligand. Indonesian *Journal of Chemistry* 16(3): 260-267.

Plotkin, B. J., Sigar, I. M., Swartzendruber, J. A., & Kaminski, A. 2018. Anaerobic growth and maintenance of mammalian cell lines. *JoVE Journal of Visualized Experiments* (137): e58049.

Prayong, P., Barusrux, S., & Weerapreeyakul, N. 2008. Cytotoxic activity screening of some indigenous Thai plants. *Fitoterapia* 79(7-8): 598-601.

Ranford, J. D., Sadler, P. J., & Tocher, D. A. 1993. Cytotoxicity and antiviral activity of transition-metal salicylato complexes and crystal structure of bis (diisopropylsalicylato)(1, 10-phenanthroline) copper (II). *Dalton Transactions* (22): 3393-3399.

Saudi, M., Zmurko, J., Kaptein, S., Rozenski, J., Neyts, J., & Van Aerschot, A. (2014). Synthesis and evaluation of imidazole-4, 5-and pyrazine-2, 3-dicarboxamides targeting dengue and yellow fever virus. *European Journal of Medicinal Chemistry* 87: 529-539.

Sharma, D., Narasimhan, B., Kumar, P., Judge, V., Narang, R., De Clercq, E., & Balzarini, J. 2009. Synthesis, antimicrobial and antiviral evaluation of substituted imidazole derivatives. *European Journal of Medicinal Chemistry* 44(6): 2347-2353.

Sucipto, T. H., Churrotin, S., Setyawati, H., Martak, F., Mulyatno, K. C., Amarullah, I. H., Soegijanto, S. 2018. New copper (II)-imidazole derivative effectively inhibits replication of DENV-2 in vero cell. *African Journal of Infectious Diseases* 12(1S): 116-119.

Sucipto, T. H., Churrotin, S., Setyawati, H. S., Mulyatno, K. C., Amarullah, I. H., Ueda, S., Bendryman, S. S. 2017. Inhibitory activity of cobalt (II)–morin complex against the replication of dengue virus type 2. *Indonesian Journal of Tropical and Infectious Disease* 6(6): 141-144.

Sucipto, T. H., & Martak, F. 2016. Synthesis of metal-organic (complexes) compounds copper (II)-imidazole for antiviral HIV candidate. *Indonesian Journal of Tropical and Infectious Disease* 6(1): 5-11.

Sucipto, T. H., Setyawati, H., Churrotin, S., Amarullah, I. H., Sumarsih, S., Wardhani, P., . . . Soegijanto, S. 2019. Anti-dengue type 2 virus activities of zinc (ii) complex compounds with 2-(2, 4-dihydroxyphenyl)-3, 5, 7-trihydroxycromen-4-one ligands in vero cells. *Indonesian Journal of Tropical and Infectious Disease* 7(5): 105-108.

Thiel, P. G., Meyer, C. J., & Marasas, W. F. 1982. Natural occurrence of moniliformin together with deoxynivalenol and zearalenone in Transkeian corn. *Journal of Agricultural and Food Chemistry* 30(2): 308-312.