

African Journal of Infectious Diseases (AJID)

ISSN 2036-0163

Journal articles



"santé est la richesse!"



Vol. 12 No. 1S (2018): Special Issue

Published: 2018-03-07

Articles

IN VITRO STUDIES ON HEME OXYGENASE-1 AND P24 ANTIGEN HIV-1 LEVEL AFTER HYPERBARIC OXYGEN TREATMENT OF HIV-1 INFECTED ON PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMCs)

Retno Budiarti, Kuntaman Kuntaman, Muhammad Nasronudin, Muhammad Guritno Suryokusumo, Siti Qamariyah Khairunisa

1-6

 [Fulltext.pdf](#)

GENOTYPING OF HUMAN PAPILLOMAVIRUS IN CERVICAL PRECANCEROUS LESION AND SQUAMOUS CELL CARCINOMA AT DR. SOETOMO HOSPITAL, SURABAYA, INDONESIA

Gondo Mastutik, Rahmi Alia, Alphania Rahniayu, Anny Setijo Rahaju, Nila Kurniasari, Suhartono Taat Putra

7-12

 [Fulltext.pdf](#)

DETERMINATION OF ENVIRONMENTAL FACTORS AFFECTING DENGUE INCIDENCE IN SLEMAN DISTRICT, YOGYAKARTA, INDONESIA

Tri Wulandari Kesetyaningsih, Sri Andarini, Sudarto Sudarto, Henny Pramoedyo

13-35

 [Fulltext.pdf](#)

ANTIVIRAL ACTIVITY OF *Justicia gendarussa* Burm.f. LEAVES AGAINST HIV-INFECTED MT-4 CELLS

Agustinus Widodo, Prihartini Widiyanti, Bambang Prajogo

36-43

 [Fulltext.pdf](#)

ACANTHAMOEBA SPS-11 PHAGOCYTOTIC ACTIVITY ON MYCOBACTERIUM LEPRAE IN DIFFERENT NUTRIENT CONDITIONS

Sepling Paling, Ratna Wahyuni, DEA Ni'matuzahroh, Dwi Winarni, M. KES Iswahyudi, Linda Astari, Dinar Adriaty, Indropo Agusni, Shinzo Izumi

44-48

 [Fulltext.pdf](#)

CD4+ AND CD8+ T-CELLS EXPRESSING INTERFERON GAMMA IN ACTIVE PULMONARY TUBERCULOSIS PATIENTS

Betty Agustina Tambunan, Hery Priyanto, Jusak Nugraha, Soedarsono Soedarsono
49-53

 [Fulltext.pdf](#)

THE ROLE OF PSYCHOLOGICAL WELL-BEING IN BOOSTING IMMUNE RESPONSE: AN OPTIMAL EFFORT FOR TACKLING INFECTION

Abdurachman Latief, Netty Herawati
54-61

 [Fulltext.pdf](#)

ANTIBACTERIAL ACTIVITY OF DRACONTOMELON DAO EXTRACTS ON METHICILLIN-RESISTANT S. AUREUS (MRSA) AND E. COLI MULTIPLE DRUG RESISTANCE (MDR)

Yuniati Yuniati, Nurul Hasanah, Sjarif Ismail, Silvia Anitasari, Swandari Paramita
62-67

 [Fulltext.pdf](#)

INCREASED APOPTOSIS SKULL OF PUPS BORN TO TOXOPLASMA GONDII-INFECTED MICE ASSOCIATED WITH INCREASED EXPRESSION OF INTERFERON GAMMA, BUT NOT TUMOR NECROSIS FACTOR ALFA

Lucia Tri Suwanti, Mufasirin Mufasirin
68-71

 [Fulltext.pdf](#)

ADDITION OF ANTI- *Toxoplasma gondii* MEMBRANE IMMUNOGLOBULIN Y TO REDUCE NECROTIC INDEX IN MICE'S LIVER

Heni Puspitasari, Lucia T. Suwanti, Mufasirin Djaeri
72-75

 [Fulltext.pdf](#)

SEROPREVALENCE AND RISK FACTOR OF TOXOPLASMOSIS IN SCHIZOPHRENIA PATIENTS REFERRED TO GRHASIA PSYCHIATRIC HOSPITAL, YOGYAKARTA, INDONESIA

Nina Difla Muflikhah, Supargiyono Supargiyono, Wayan Tunas Artama
76-82

 [Fulltext.pdf](#)

CONCOMITANT SEXUALLY TRANSMITTED DISEASES IN PATIENTS WITH DIAGNOSED HIV/AIDS: A RETROSPECTIVE STUDY

Densy Violina Harnanti, Afif Nurul Hidayati, Muhammad Miftahussurur
83-89

[Fulltext.pdf](#)

RISK FACTORS OF VULVOVAGINAL CANDIDIASIS IN DERMATO-VENERELOGY OUTPATIENTS CLINIC OF SOETOMO GENERAL HOSPITAL, SURABAYA, INDONESIA

Dharin Serebrina Arfiputri, Afif Nurul Hidayati, Samsriyaningsih Handayani, Evy Ervianti

90-94

[Fulltext.pdf](#)

COMPARISON OF ANTI BACTERIAL EFFICACY OF PHOTODYNAMIC THERAPY AND DOXYCYCLINE ON AGGREGATIBACTER ACTINOMYCETEMCOMITANS

Ernie Maduratna Setiawatie, Vina Puji Lestari, Suryani Dyah Astuti

95-103

[Fulltext.pdf](#)

EVALUATION OF THE ANTIGENICITY AND IMMUNOGENICITY OF *Eimeria tenella* BY REPRODUCTIVE INDEX AND HISTOPATHOLOGICAL CHANGES OF CECAL COCCIDIOSIS VIRULENT LIVE VACCINE IN BROILER CHICKENS

Endang Suprihati, Muchammad Yunus

104-110

[Fulltext.pdf](#)

DETERMINATION OF EFFECTIVE DOSE OF ANTIMALARIAL FROM CASSIA SPECTABILIS LEAF ETHANOL EXTRACT IN PLASMODIUM BERGHEI-INFECTED MICE

Wiwied Ekasari, Tutik Sri Wahyuni, Heny Arwati, Nindya T. Putri

111-115

[Fulltext.pdf](#)

A NEW COPPER (II)-IMIDAZOLE DERIVATIVE EFFECTIVELY INHIBITS REPLICATION OF DENV-2 IN VERO CELL

Teguh Hari Sucipto, Siti Churrotin, Harsasi Setyawati, Fahimah Martak, Kris Cahyo Mulyatno, Ilham Harlan Amarullah, Tomohiro Kotaki, Masanori Kameoka, Masanori Kameoka, Subagyo Yotopranoto, Soegeng Soegijanto

116-119

[Fulltext.pdf](#)

COMPARISON OF MULTIPLEX SINGLE ROUND PCR AND MICROSCOPY IN DIAGNOSIS OF AMOEBIASIS

BS Sri-Hidajati, Sukmawati Basuki, Suhintam Pusarawati, Kusmartisnawati Kusmartisnawati, Lynda Rossyanti, Sri Wijayanti Sulistyowati, Dwi Peni Kartikasari, Heny Arwati, Indah Tantular, Alpha Fardah, Andy Darma, Retno Handajani, Subijanto Marto Soedarmo

120-126

[Fulltext.pdf](#)

CLONING AND EXPRESSION OF MCE1A GENE FROM MYCOBACTERIUM TUBERCULOSIS BEIJING AND H37RV STRAIN FOR VACCINE CANDIDATE DEVELOPMENT

Desi Indriarini, Andriansjah Rukmana, Andi Yasmon

127-132

 [Fulltext.pdf](#)

EFFECT OF VARYING INCUBATION PERIODS ON CYTOTOXICITY AND VIRUCIDAL ACTIVITIES OF *Justicia gendarussa* Burm.f. LEAF EXTRACT ON HIV-INFECTED MOLT-4 CELLS

Prihartini Widiyanti, Bambang Prajogo, Agustinus Widodo

133-139

 [Fulltext.pdf](#)

IN SILICO SCREENING AND BIOLOGICAL EVALUATION OF THE COMPOUNDS OF *Justicia gendarussa* LEAVES EXTRACT AS INTERFERON GAMMA INDUCER: A STUDY OF ANTI HUMAN IMMUNODEFICIENCY VIRUS (HIV) DEVELOPMENT

Restry Sinansari, Bambang EW Prajogo, Prihartini Widiyanti

140-147

 [Fulltext.pdf](#)

ISOLATION AND IDENTIFICATION OF BRUCELLA SUIIS IN PIGS AS ZONOTIC DISEASE IN ENDEMIC AREAS OF EAST JAVA, INDONESIA

Emy S Koestanti, Wiwik Misaco, Sri Chusniati, Lilik Maslachah

148-151

 [Fulltext.pdf](#)

Intructions for Authors

INSTRUCTIONS FOR AUTHORS

Babatunde O Olagunju

152-158

 [FullText.PDF](#)

[Make a Submission](#)

Information

[For Readers](#)

[For Authors](#)

[For Librarians](#)

Keywords



Most Read Articles (last 30 days)

KNOWLEDGE AND COMPLIANCE TO PRACTICE OF PREVENTIVE MEASURES TO COVID-19 AMONG NURSES IN A SELECTED TERTIARY HOSPITAL IN SOUTH-SOUTH, NIGERIA

👁 20

EMERGENCE OF NEW STRAINS OF SARS-COV-2: AFRICA'S FATE AND ITS PREPAREDNESS AGAINST COVID-19 INFECTION WAVES

👁 20

PREVALENCE OF TUBERCULOSIS, DRUG-RESISTANT TUBERCULOSIS AND HIV/TB CO-INFECTION IN ENUGU, NIGERIA.

👁 18

EXPRESSION OF IMMUNOGLOBULIN, GRANZYME-B AND PERFORIN AGAINST Ag85A AND Ag85B PROTEINS OF MYCOBACTERIUM TUBERCULOSIS IN BALB/C MICE

👁 18

RDT- AND MICROSCOPIC-BASED TRENDS OF MALARIA AMONG LOCAL AND MIGRANT POPULATIONS IN THE PROVINCE OF CENTRAL KALIMANTAN, INDONESIA DURING 2017-2020

👁 18



All articles of the African Journal of Infectious Diseases (AJID) are published under the terms of the [Attribution 4.0 International \(CC BY 4.0\)](#), which allows users to copy, distribute and transmit an article, adapt the article and make commercial use of the article. The CC BY license permits commercial and non-commercial re-use of an open access article, as long as the author is properly attributed.

OJS Support, and Customization by | [OJS-Services.com](#)

Editorial Team

Managing Editor

Prof. Cyprian O. Onyeji, Department of Pharmaceutical and Medicinal Chemistry Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka. Nigeria. E-mail: cyprian.onyeji@unn.edu.ng

Editorial Assistants

Ms Omolade Olaboye, African Journal of Infectious Diseases COJA VILLA, 7, Road 1, Otun Maye Square, Ajebamidele, Ile-Ife, Osun State, Nigeria. E-mail: omolade@athmsi.org, Nigeria

Mr. Hammed Ibraheem, African Journal of Infectious Diseases, COJA VILLA, 7, Road 1, Otun Maye Square, Ajebamidele, Ile-Ife, Osun State, Nigeria. E-mail: hammed@athmsi.org, Nigeria

Associate Editors

Prof. Ademola OLANIRAN, University of KwaZulu-Natal, Durban, South Africa E-mail: olanirana@ukzn.ac.za, South Africa

Prof. Francesca MANCIANTI, Faculty of Medicine, University of Pisa, Italy E-mail: francesca.mancianti@unipi.it, Italy

Dr. Emel SONMEZ, Anadolu University, Eskisehir, Turkey E-mail: emls222224@gmail.com, Turkey

Prof. wang HUI, Chinese Academy of Agricultural Sciences, Gansu, China. E-mail: wanghui01@caas.cn, China

Editors-in-Chief

Prof. Anthony O. ONIPEDE, Department of Medical Microbiology & Parasitology, Faculty of Basic Medical Sciences, College of Health sciences, Obafemi Awolowo University, Ile-ife, Osun-State, Nigeria. E-mail: aonipede@oauife.edu.ng, Nigeria

Dr. Gbola OLAYIWOLA, Department of Clinical Pharmacy, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, Nigeria. E-mail: gbolaolayiwola@yahoo.com, Nigeria

Editorial Board

Dr. Saajida Mahomed, University of KwaZulu-Natal, Durban, South Africa. E-mail: mahomeds@ukzn.ac.za

Dr. Ahmed Adu-Oppong, Georgia Southern University, USA E-mail: aaduoppong@georgiasouthern.edu, United States

Prof. Vincent P. K. Titanji, University of Buea, Cameroon. E-mail: vpk.titanji@yahoo.com, Cameroon

Professor Phyllis J KANKI, Department of Immunology & Infectious Disease Harvard School of Public Health, USA. E-mail: pkanki@hsph.harvard.edu, United States

Dr. Celsus Sente, Makerere University, Kampala, Uganda. E-mail: csenhte@covab.mak.ac.ug, Uganda

Dr. Babajide sadiq, Florida A&M University, USA. E-mail: babajidesadiq@yahoo.com, United States

Dr Sharlene Govender, Department of Biochemistry & Microbiology Nelson Mandela Metropolitan University Port Elizabeth South Africa. E-mail: sharlene.govender@nmmu.ac.za, South Africa

Dr. Alok Kumar, University of the West Indies, Cave Hill, Jamaica. E-mail: alokkumar.uwichill@gmail.com

Prof. Chrispinus Mulambalah Siteti, Moi University, School of Medicine, Kitale, Kenya. E-mail: csmulambalah@gmail.com

Prof. Megbaru Alemu, Bahir Dar University Department of Microbiology, Immunology & Parasitology, Ethiopia. E-mail: mgbeyney@gmail.com, Ethiopia

Dr. Balram Ji Omar, Department of Microbiology All India Institute Of Medical Sciences Rishikesh, India. E-mail: drbalramaiims@gmail.com, India

Dr. Josyline Kaburi, University of Nairobi, Kenya. E-mail: jeirindi@kemri.org, Kenya

Dr Ezekiel Olugbenga Akinkunmi, Department of Pharmarmaceutics, Obafemi Awolowo Unversity, Ile-Ife, Nigeria. E-mail: akinkeroo@yahoo.com, Nigeria

Dr. Frank Onyambu, Kenya Medical Research Institute, PO Box 29408 NAIROBI -00100, Kenya. E-mail: frank.onyambu@iscb.org, Kenya

Dr. Suresh G. Joshi, Division of Infectious Diseases, Thomas Jefferson University, Philadelphia, PA 19107, USA' E-mail: surejoshi@yahoo.com

[Make a Submission](#)

Information

[For Readers](#)

[For Authors](#)

[For Librarians](#)

Keywords



Most Read Articles (last 30 days)

KNOWLEDGE AND COMPLIANCE TO PRACTICE OF PREVENTIVE MEASURES TO COVID-19 AMONG NURSES IN A SELECTED TERTIARY HOSPITAL IN SOUTH-SOUTH, NIGERIA

👁 20

EMERGENCE OF NEW STRAINS OF SARS-COV-2: AFRICA'S FATE AND ITS PREPAREDNESS AGAINST COVID-19 INFECTION WAVES

👁 20

PREVALENCE OF TUBERCULOSIS, DRUG-RESISTANT TUBERCULOSIS AND HIV/TB CO-INFECTION IN ENUGU, NIGERIA.

👁 18

EXPRESSION OF IMMUNOGLOBULIN, GRANZYME-B AND PERFORIN AGAINST Ag85A AND Ag85B PROTEINS OF MYCOBACTERIUM TUBERCULOSIS IN BALB/C MICE

👁 18

RDT- AND MICROSCOPIC-BASED TRENDS OF MALARIA AMONG LOCAL AND MIGRANT POPULATIONS IN THE PROVINCE OF CENTRAL KALIMANTAN, INDONESIA DURING 2017-2020

👁 18



All articles of the African Journal of Infectious Diseases (AJID) are published under the terms of the [Attribution 4.0 International \(CC BY 4.0\)](https://creativecommons.org/licenses/by/4.0/), which allows users to copy, distribute and transmit an article, adapt the article and make commercial use of the article. The CC BY license permits commercial and non-

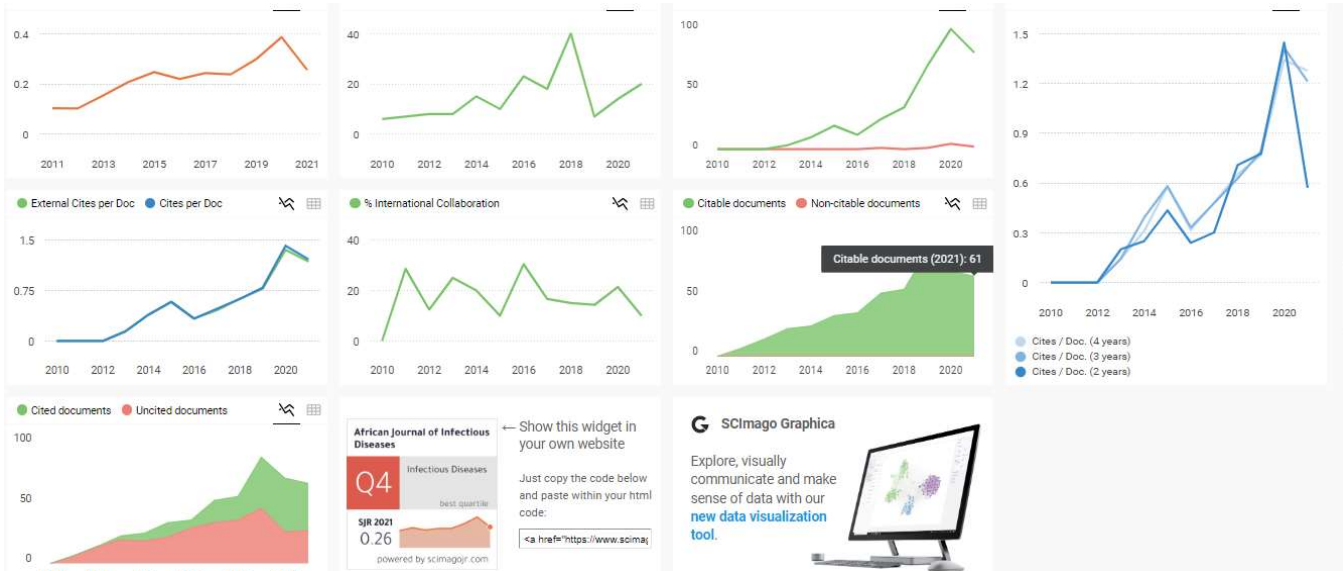
commercial re-use of an open access article, as long as the author is properly attributed.

OJS Support, and Customization by | [OJS-Services.com](https://www.ojs-services.com)

BUKTI SCOPUS

African Journal of Infectious Diseases

COUNTRY Nigeria 	SUBJECT AREA AND CATEGORY Medicine Infectious Diseases	PUBLISHER Obafemi Awolowo University	H-INDEX <h1 style="font-size: 2em;">14</h1>
PUBLICATION TYPE Journals	ISSN 20060165	COVERAGE 2010-2021	INFORMATION Homepage How to publish in this journal cyprian.onyeji@unn.edu.ng



A NEW COPPER (II)-IMIDAZOLE DERIVATIVE EFFECTIVELY INHIBITS REPLICATION OF DENV-2 IN VERO CELL

Teguh Hari Sucipto^{1*}, Siti Churrotin¹, Harsasi Setyawati², Fahimah Martak³, Kris Cahyo Mulyatno¹, Ilham Harlan Amarullah¹, Tomohiro Kotaki⁴, Masanori Kameoka⁴, Subagyo Yotopranoto¹, and Soegeng Soegijanto¹

¹Dengue Study Group, Institute of Tropical Disease, Airlangga University, Kampus C Jl. Mulyorejo, Surabaya, East Java, Indonesia, 60115; ²Department of Chemistry, Faculty of Science and Technology, Airlangga University, Kampus C Jl. Mulyorejo, Surabaya, East Java, Indonesia, 60115; ³Department of Chemistry, Faculty of Mathematic and Natural Science, Sepuluh Nopember Institute of Technology, Kampus Sukolilo Jl. Raya ITS, Surabaya, East Java, Indonesia, 60111; ⁴Department of International Health, Kobe University Graduate School of Health Sciences, 7-10-2 Tomogaoka, Suma-ku, Kobe, Hyogo 654-0142, Japan

*Corresponding Author E-mail: teguhharisucipto@gmail.com

Article History

Received: Feb. 02, 2017

Revised Received: Aug. 18, 2017

Accepted: Aug. 18, 2017

Published Online: March. 07, 2018

Abstract

Background: Dengue is a kind of infectious disease that was distributed in the tropical and sub-tropical areas. To date, there is no clinically approved dengue vaccine or antiviral for humans, even though there have been great efforts towards this end. Therefore, finding the effective compound against dengue virus (DENV) replication is very important. Among the complex compounds, copper(II)-imidazole derivatives are of interest because of their biological and medicinal benefits.

Materials and Methods: In the present study, antiviral activity of [Cu(2,4,5-triphenylimidazole)₂]_n, was evaluated against different stages of dengue virus type 2 (DENV-2) replication in Vero cell using focus forming unit reduction assay and quantitative ELISA.

Results: [Cu(2,4,5-triphenylimidazole)₂]_n inhibited DENV-2 replication in Vero cells with IC₅₀ = 2.3 µg/ml and SI= 19.42 when cells were treated 2 days after virus infection, whereas its CC₅₀ for cytotoxicity to Vero cells was 44.174 µg/ml.

Conclusion: The compound has high anti-DENV2 activity, less toxicity, and a high possibility to be considered a drug candidate.

Keywords: DENV-2, Antiviral activity, Vero cell, [Cu(2,4,5-triphenylimidazole)₂]_n

Introduction

Dengue is a kind of infectious disease that is distributed in the tropical and sub-tropical areas (Bhatt et al., 2013; Franco et al., 2010; Guzman et al., 2010). Dengue is transmitted to human by *Aedes aegypti*. More than 250,000-500,000 cases dengue infection occurred in the world every years (Bharaj et al., 2008; Reiter, 2001). Four distinct serotypes were reported, DENV-1, DENV-2, DENV-3, and DENV-4 (Balmaseda et al., 2006; Holmes and Twiddy, 2003). Indonesia is one of the largest countries in the dengue-endemic region worldwide (Fahri et al., 2013; Kotaki et al., 2014; Kotaki et al., 2016; Setiati et al., 2006). In Indonesia, dengue occurred for the first time as an outbreak in Jakarta and Surabaya, in 1968 (Sumarmo, 1987). To date, there is no clinically approved dengue vaccine or antiviral for humans, even though there have been great efforts towards this end.

2,3,5-triphenylimidazole, is a derivate of imidazole. The strong therapeutic properties of imidazole-containing drugs have encouraged medicinal chemists to synthesize a large number of novel chemotherapeutic agents comprising this entity. N5-(4-fluorophenyl)-N4-(2-(pyridin-4-yl)benzyl)-1*H*-imidazole-4,5-dicarboxamide, a derivate of imidazole, was reported anti-DENV activity (Saudi et al., 2014).

The complex compound forms as a result of metal and organic compound reaction. It can be used as an anti-inflammatory (Agotegaray et al., 2012), antimicrobial (Carcelli et al., 1995), antifungal, antibacterial (Arjmand et al.,

2005), antivirus (Ranford et al., 1993). For example, Pt-acesulfame compound showed a good inhibition of dengue virus replication mainly at 200 μM , when compared to the vehicle-treated cells (Cavicchioli et al., 2010). Therefore, in this research we sought to screen Cu(II)-Imidazole for dengue type 2 inhibition.

Materials and Methods

Materials

Chemical reagents used in this research include copper(II)chloride dihydrate ($\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$) (Merck 99.0%), N,N-dimethyl formamide (DMF) (Merck 99.8%), 2,4,5-triphenylimidazole ligand (Sigma-Aldrich 90%), dimethyl sulfoxide (DMSO) (Sigma-Aldrich 99.8%) and ethanol (Sigma-Aldrich 96%).

Vero cells used for screening antiviral activity were incubated at 37 °C in Eagle's minimum essential medium supplemented with 10% fetal bovine serum. Dengue virus type 2 (DENV-2) strains from Surabaya, Indonesia and cell monolayers were examined for the presence of viral antigen by immunostaining with a flavivirus-specific monoclonal antibody (D1-4G2; American Type Culture Collection, Manassas, VA).

Methods

Synthesis of $[\text{Cu}(\text{2,4,5-triphenylimidazole})_2]_n$

The compound was synthesized using solvothermal method with heating time of 3 hours at temperature of 120°C (Han et al., 2012).

Cytotoxicity assay

Using WST-1 cell proliferation reagent (Roche Applied Science, Mannheim, Germany) (Chew et al., 2015). Vero cells (1×10^5 cells/ml) were seeded in 96-well plate at 37 °C in 5% CO_2 overnight. Following serial dilution 100 μl of the compound was incubated with Vero cells for 24 h. 10 μl of Cell Proliferation Reagent WST-1 was added into each well, incubated for 1 hour at 37 °C. The plate was read at 450 nm (main filter) and 655 nm (reference filter) using an ELISA reader (iMark™ Microplate Absorbance Reader).

In vitro study

Vero cells (1×10^5 cells/ml) were also seeded in 96-well plate at 37 °C in 5% CO_2 overnight. DENV-2 virus solution (MOI of 2) was prepared in MEM containing 10% FBS. Another serially diluted compound was added and incubated 37 °C for 1 hour. The supernatant was discarded and the pellet was washed with sterilized PBS three times, then MEM containing 10% FBS was added, followed by serially diluted test compound to the Vero cells incubated at 37 °C for 2 days. The supernatant was used for ELISA at 450 nm (Wang et al., 2009) using an ELISA reader (iMark™ Microplate Absorbance Reader).

Results and Discussions

Cytotoxicity of $[\text{Cu}(\text{2,4,5-triphenylimidazole})_2]_n$ to DENV-2-infected Vero cells

The result of the cell proliferation assay at 1 hour is shown in Figure 1. The compound, when added to Vero cells exhibited cytotoxic effects at $\text{CC}_{50} = 44.74 \mu\text{g/ml}$. One percent DMSO (negative control) did not show any cytotoxic effects against Vero cells.

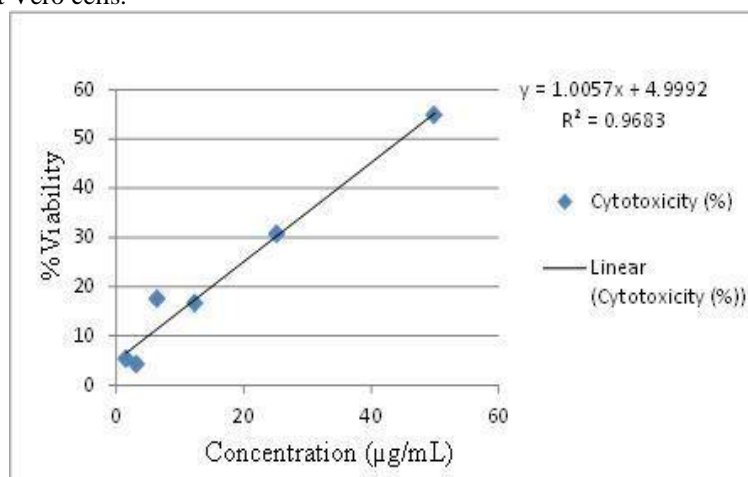


Figure 1: Linear curve for cytotoxicity of $[\text{Cu}(\text{2,4,5-triphenylimidazole})_2]_n$

CC_{50} is cytotoxicity level of $[Cu(2,4,5\text{-triphenylimidazole})_2]_n$ (compound) to cause death to 50% of Vero cells. IC_{50} was calculated from regression linier curve; $y = 1.0057x + 4.9992$ with the axis (x) is concentration of compound and ordinate (y) is %viability.

Inhibition of DENV-2 Infection by $[Cu(2,4,5\text{-triphenylimidazole})_2]_n$ *in vitro*

The inhibitory ability of the compound against DENV-2 infection was determined via ELISA method. The compound was incubated with DENV-2 for 1 hour prior addition to Vero cells. The compound exhibited adsorption inhibitory activity against DENV-2 at $IC_{50} = 2.3 \mu\text{g/ml}$ (SI value of 19.42). Percentage inhibition increased with increasing concentrations of compound (Figure 2). This indicates that dengue virus replication was inhibited. The inhibition at IC_{50} was not significantly high ($p < 0.005$) compared to that of the metal-free imidazole ($IC_{50} = 0.13 \mu\text{g/ml}$). But, the metal-free imidazole more toxic for Vero cells ($CC_{50} = 5.03 \mu\text{g/ml}$) (Sucipto et al., 2017). However, studies on the compound of imidazole-4,5- showed higher antiviral potency against yellow fever virus (YFV) than dengue virus (DENV). This bioactivity may be within the imidazole series of a 'para'-attachment of a heterocycle to its 'C' (Saudi et al., 2014).

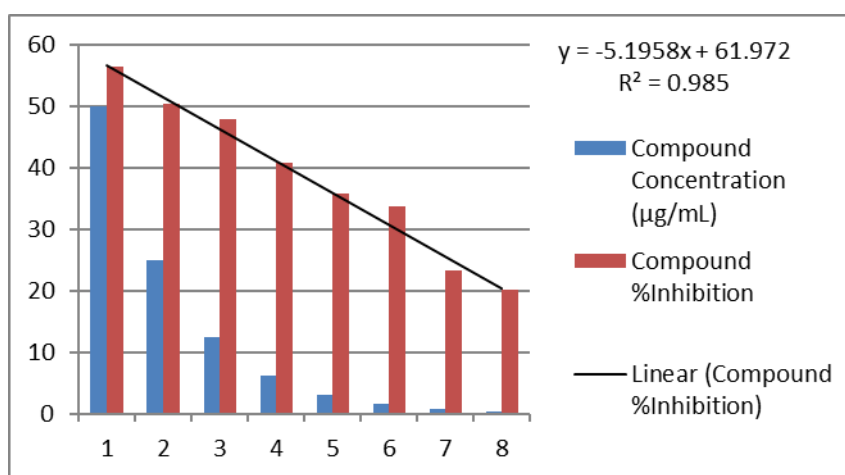


Figure 2: Inhibition curve of $[Cu(2,4,5\text{-triphenylimidazole})_2]_n$ to DENV-2

IC_{50} (maximal inhibitory concentration) is measure of the effectiveness of a substance in inhibiting a specific DENV-2. In this curve was used 8 concentration; 50 $\mu\text{g/ml}$, 25 $\mu\text{g/ml}$, 12.5 $\mu\text{g/ml}$, 6.25 $\mu\text{g/ml}$, 3.13 $\mu\text{g/ml}$, 1.56 $\mu\text{g/ml}$, 0.78 $\mu\text{g/ml}$ and 0.39 $\mu\text{g/ml}$. IC_{50} was calculated from regression linier curve; $y = -5.1958x + 61.972$.

Acknowledgments

This work was supported by the joined program of the Japan Initiative for Global Research Network on Infectious Disease (J-GRID); Research Grant Mandat Universitas Airlangga (HRMUA); Institute of Tropical Disease (ITD) the Center of Excellence (COE) program by the Ministry of Research and Technology (RISTEK) Indonesia.

Conflict of Interest: Authors declare that they have no competing interest.

References

1. Agotegaray, M.A., Dennehy, M., Boeris, M.A., Grela, M.A., Burrow, R. A., and Quinzani, O.V. (2012). Therapeutic properties, SOD and catecholase mimetic activities of novel te,ary copper(II) complexes of the anti-inflammatory drug fenoprofen with imidazole and caffeine. *Polyhedron.*, **34**: 74-83
2. Arjmand, F., Mohani, B., and Ahmad, S. (2005). Synthesis, antibacterial, antifungal activity and interaction of CT-DNA with a new benzimidazole derived Cu(II) complex. *Europ. J. Med. Chem.*, **40**: 1103-1110
3. Balmaseda, A., Hammond S.N., Pérez, L., Tellez Y., Saborío, S.I., Mercado, J.C., Cuadra, R., Rocha, J., Pérez, M.A., Silva, S., Rocha, C., and Harris, E. (2006). Serotype-specific differences in clinical manifestations of dengue. *Am. J. Trop. Med. Hyg.*, **74**: 440-456
4. Bharaj, P., Chahar, H.S., Pandey, A., Diddi, K., Dar, L., Guleria, R., Kabra, S.K., and Broor, S. (2008). Concurrent infections by all four dengue virus serotypes during an outbreak of dengue in 2006 in Delhi, India. *Virol. J.*, **5**: 1-5

5. Bhatt, S., Gething, P.W., Brady, O.J., Messina, J.P., Farlow, A.W., Moyes, C.L., Drake, J.M., Brownstein, J.S., Hoen, A.G., Sankoh, O., Myers, M.F., George, D.B., Jaenisch, T., Wint, G.R.W., Simmons, C.P., Scott, T.W., Farrar, J.J., and Hay, S.I. (2013). The global distribution and burden of dengue. *Nature*, **496**: 504-507
6. Carcelli, M., Mazza, P., Pelizzi, C., Pelizzi, G., and Zani, F. (1995). Antimicrobial and genotoxic activity of 2,6-diacetylpyridine bis(Acylhydrazones) and their complexes with some first transition series metal ions. X-ray crystal structure of dinuclear copper(II) complex. *J. Inorg. Biochem.*, **57**: 43-62
7. Cavicchioli, M., Massabni, A.C., Heinrich, T.A., Costa-Neto, C.M., Abrão, E.P., Fonseca, B.A.L., Castellano, E.E., Corbi, P.P., Lustrri, W.R., and Leite, C.Q.F. (2010). Pt(II) and Ag(I) complexes with acesulfame: Crystal structure and a study of their antitumor, antimicrobial and antiviral activities. *J. Inorg. Biochem.*, **104**: 533-540
8. Chew, M.F., Tham, H.W., Rajik, M., and Sharifah, S.H. (2015). Anti-dengue virus serotype 2 activity and mode of action of a novel peptide. *J. App. Microbio.*, **119**: 1170-1180
9. Fahri, S., Yohan, B., Trimarsanto, H., Sayono, S., Hadisaputro, S., Dharma, E., Syafruddin, D., and Sasmono, R.T. (2013). Molecular surveillance of dengue in Semarang, Indonesia revealed the circulation of an old genotype of dengue virus serotype-1. *Plos Neg. Trop. Dis.*, **7**: 1-12
10. Franco, L., Caro, A.D., Carietti, F., Vapalahti, O., Renaudat, C., Zeller, H., Tenorio, A. (2010). Recent expansion of dengue virus serotype 3 in West. *Eur. J. Inf. Dis. Epid. Prev. Con.*, **73-76**
11. Guzman, M.G., Halstead, S.B., Artsob, H., Buchy, P., Farrar, J., Gubler, D.J., Hunsperger, E., Kroeger, A., Margolis, H.S., Martinez, E., Nathan, M.B., Pelegrio, J.L., Simmons, C., Yoksan, S., and Peeling, R.W. (2010). Dengue: a continuing global threat. *Nature*, **S7-S16**
12. Han, S., Lough, A. J., and Kim, J. C. (2012). Synthesis, Crystal Structures and Properties of Macrocyclic Copper(II) Complexes Containing Imidazole Pendants. *Bull. Korean Chem. Soc.*, **33**: 2381-2384
13. Holmes, E.C., and Twiddy, S.S. (2003). The origin, emergence and evolutionary genetics of dengue virus. *Inf. Gen. Evol.*, **3**: 19-28
14. Kotaki, T., Yamanaka, A., Mulyatno, K.C., Churrotin, S., Labiqah, A., Sucipto, T.H., Soegijanto, S., Kameoka, M., Konishi, E. (2014). Continuous dengue type 1 virus genotype shifts followed by co-circulation, clade shifts and subsequent disappearance in Surabaya, Indonesia, 2008-2013. *Inf. Gen. Evol.*, **28**: 48-54
15. Kotaki, T., Yamanaka, A., Mulyatno, K.C., Churrotin, S., Sucipto, T.H., Labiqah, A., Ahwanah, N.L.F., Soegijanto, S., Kameoka, M., Konishi, E. (2016). Divergence of the dengue virus type 2 cosmopolitan genotype associated with two predominant serotype shifts between 1 and 2 in Surabaya, Indonesia, 2008-2014. *Inf. Gen. Eval.*, **37**: 88-93
16. Ranford, J.D., Sadler, P.J., and Tocher, D.A. (1993). Cytotoxicity and antiviral activity of transition-metal salicylate complexes and crystal structure of bis(diisopropylsalicylato)(1,10-phenanthroline) copper(II). *J. Chem. Soc.*, **3**: 3393-3399
17. Reiter, P. (2001). Climate change and mosquito-borne disease. *Environ. Health Perspect.*, **109**: 141-161
18. Saudi, M., Zmurko, J., Kaptein, S., Rozenski, J., Neyts, J., and Aerschot, A.V. (2014). Synthesis and evaluation of imidazole-4,5- and pyrazine-2,3- dicarboxamides targeting dengue and yellow fever virus. *Europ. J. Med. Chem.*, **87**: 529-539
19. Setiati, T.E., Wagenaar J.F.P., Krul, M.D., Mairuhu, A.T.A., Gorp, E.C.M., and Soemantri, A. (2006). Changing epidemiology of dengue haemorrhagic fever in Indonesia. *Dengue Bull.*, **30**:1-14
20. Sucipto, T.H., Churrotin, S., Setyawati, H., Kotaki, T., Martak, F., Soegijanto, S. (2017). Antiviral activity of copper(II)chloride dehydrate against dengue virus type-2 in vero cell. *Indonesian J. Trop. Inf. Dis.*, **6**: 90-93
21. Sumarmo (1987). Dengue haemorrhagic fever in Indonesia. *Southeast Asian J. Trop. Med. Pub. Health.*, **18**: 269-274
22. Wang, Q.Y., Patel S.J., Vangrevelinghe, E., Xu, H.Y., Rao, R., Jaber, D., Schul, W., Gu, F., Heudi, O., Ma, N.L., Poh, M.K., Phong, W.Y., Keller, T.H., Jacoby, E., and Vasudevan, S.G. (2009). A Small-Molecule Dengue Virus Entry Inhibitory. *Antimicrob. Agents Chemother.*, **53**: 1823-1831.